



# Anaemia & iron deficiency

Clementine Stubbs, ST5<sup>+</sup>

Final FRCA Teaching

12<sup>th</sup> May 2021

# The scope of the problem

- + Prevalence of anaemia worldwide = 32.9%!
- + Anaemia accounts for 8.8% of total disease burden of all conditions
- + 40% of patients presenting for major surgery are anaemic



# Perioperative consequences!



- + Cancellation & delayed treatment
- + Increased length of hospital stay & ICU stay
- + Increased cardiac events (MI)
- + Increased respiratory, urinary & wound infections
- + Increased thromboembolic events
- + Increased all cause morbidity & mortality
- + Increased need for autologous blood transfusion & its risks

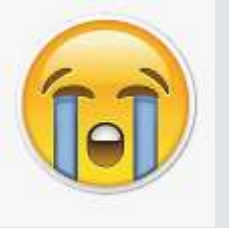


# Complications of blood transfusion

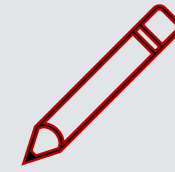
	Immunological	Non-immunological
Immediate	<ul style="list-style-type: none"><li>• Haemolytic transfusion rxn</li><li>• Febrile non-haemolytic transfusion rxn</li><li>• Anaphylaxis</li><li>• Urticaria</li></ul>	<ul style="list-style-type: none"><li>• Hypothermia</li><li>• Coagulopathy</li><li>• Hypocalcaemia</li><li>• Hyperkalaemia</li><li>• Metabolic acidosis</li><li>• TACO</li></ul>
Delayed	<ul style="list-style-type: none"><li>• Delayed haemolytic transfusion rxn</li><li>• Delayed febrile rxn</li><li>• TRALI</li></ul>	<ul style="list-style-type: none"><li>• Transmission of infections: viral (HIV, hep C/B/A), bacterial (<i>S. epidermidis</i>), parasite (malaria)</li></ul>

# But really...

- + September 2019 CRQ question: Perioperative anaemia and blood loss (pass rate 55.7%)
  - + “This question is very relevant to anaesthetic practice and yet performed surprisingly poorly.”
- + NISOA: Preoperative anaemia, Blood transfusion, Jehovah’s witnesses and blood conservation strategies
- + Final SOE 2, anaemia is a common comorbidity, e.g. SOE 2 example on the RCoA website



# Learning objectives



= examinable!

- + Define anaemia
- + Recall the physiological effects of anaemia
- + Classify causes of anaemia according to the underlying disease process and histologically
- + Describe iron absorption, transport, storage & haemostasis
- + **Select and interpret relevant investigations to diagnose anaemia and iron deficiency**
- + **Formulate an appropriate perioperative management plan for patients presenting with anaemia & iron deficiency**

# Definition of anaemia

## WHO & NICE

- + Men Hb <130 g/l
- + Women Hb <120 g/l



## PQIP & Anaesthesia

- + Both Hb <130 g/l

# Physiological effects



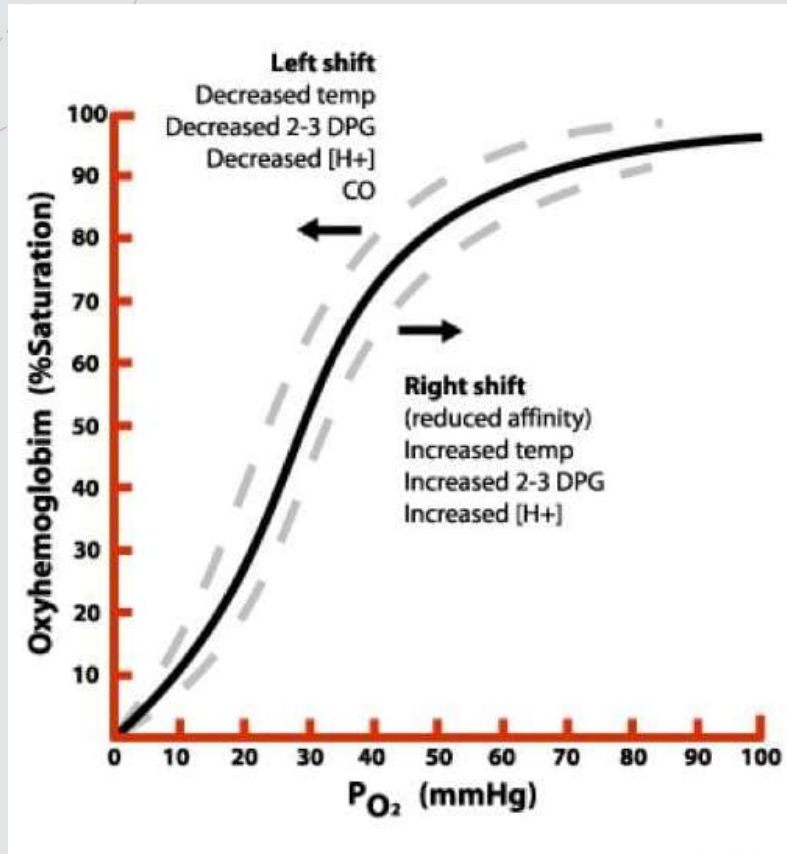
$$CaO_2 = 1.34 \times \mathbf{[Hb]} \times \text{sats} + 0.03 \times [PaO_2]$$

$$DO_2 = CaO_2 \times CO$$





# Physiological effects



- + ↑ Cardiac output
- + ↑ O<sub>2</sub> extraction
- + Redistribution
- + ↑ 2,3-DPG & hydrogen ions

# Signs & symptoms



SIGNS	SYMPTOMS
pallor (general & conjunctival)	fatigue / lethargy
tachycardia	palpitations
syncope	dizziness
flow murmur	angina
signs of high output cardiac failure	dyspnoea
koilonychia (IDA)	Intermittent claudication

# Classification of anaemia - underlying disease process

Deficiency	Haemolysis	Marrow failure
<ul style="list-style-type: none"><li>• Iron</li><li>• B<sub>12</sub></li><li>• Folic acid</li><li>• Erythropoietin</li></ul>	<ul style="list-style-type: none"><li>• <u>Intrinsic</u>: sickle cell, thalassaemia, G6PD, hereditary spherocytosis</li><li>• <u>Extrinsic</u>: immune (SLE, hypersplenism, lymphoma), non-immune (DIC, drugs, infection (Clostridium tetani))</li></ul>	<ul style="list-style-type: none"><li>• Aplasia</li><li>• Suppression: malignancy, drugs, infection</li><li>• Dyserthropoiesis (myelodysplastic syndrome)</li></ul>

**& Blood loss:** acute (trauma / GI), chronic (parasite / NSAIDs)

# Classification of anaemia - histological

<b>Hypochromic, microcytic</b>	<b>Normochromic normocytic</b>	<b>Macrocytic</b>
<ul style="list-style-type: none"><li>• Iron deficiency</li><li>• Occult GI / gynae loss</li><li>• Thalassaemia</li></ul>	<ul style="list-style-type: none"><li>• Anaemia of chronic disease</li><li>• Acute blood loss</li><li>• Hypothyroidism</li><li>• Bone marrow failure</li><li>• Haemolysis</li></ul>	<ul style="list-style-type: none"><li>• Megaloblastic: B<sub>12</sub>/folate deficiency (MCV &gt;110 fl)</li><li>• Non-megaloblastic: pregnancy, alcohol, drugs (MCV 100–110 fl)</li></ul>

# Periop events that worsen effects of anaemia



REDUCED O <sub>2</sub> DELIVERY	INCREASED O <sub>2</sub> DEMAND
Hypovolaemia	Pain
Cardiac depressant drugs	Fever
Atelectasis	Shivering
pneumonia	Stress response
thromboembolism	
Surgical blood loss	
Hypothermia	

# Iron deficiency

- + Most common & widespread nutritional deficiency
- + 2 billion people worldwide are deficient
- + Leading cause of anaemia
- + Important roles besides erythropoiesis!
  - + Oxygen transport
  - + Electron transfer reactions
  - + Mitochondrial respiration
  - + Gene regulation
  - + Cellular immunity

# Iron distribution

+ Total body content:

+ men 3-4g

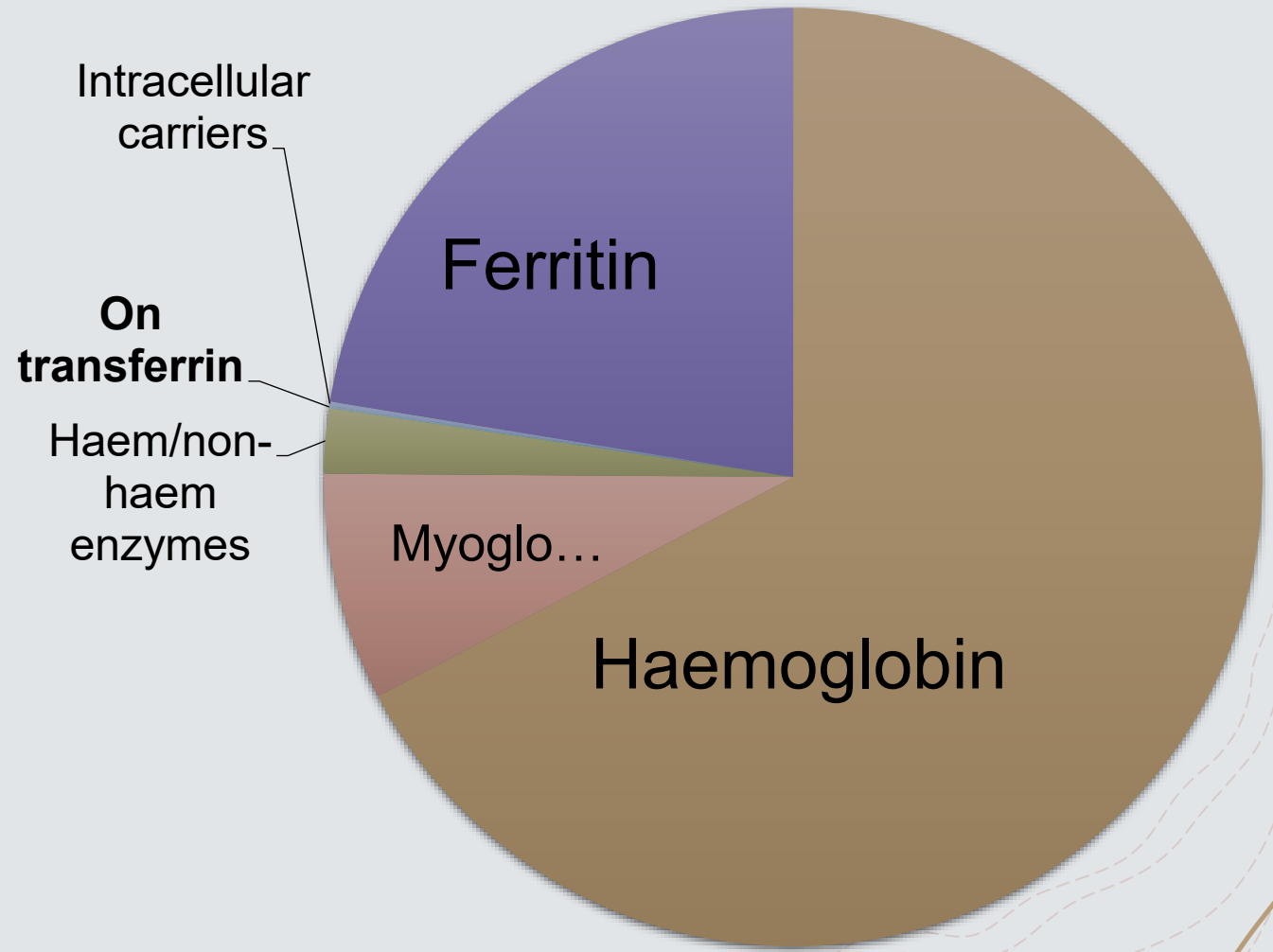
+ women 2.5g

+ Bone marrow needs:

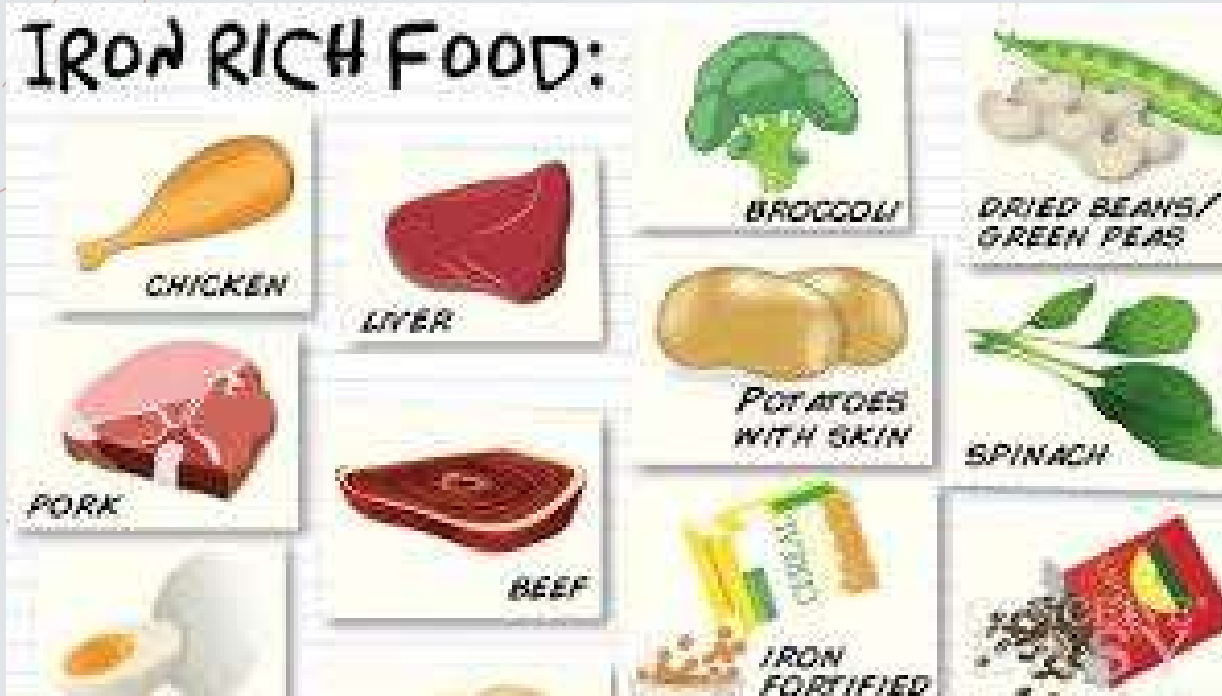
+ 25 mg/day

+ Dietary absorption:

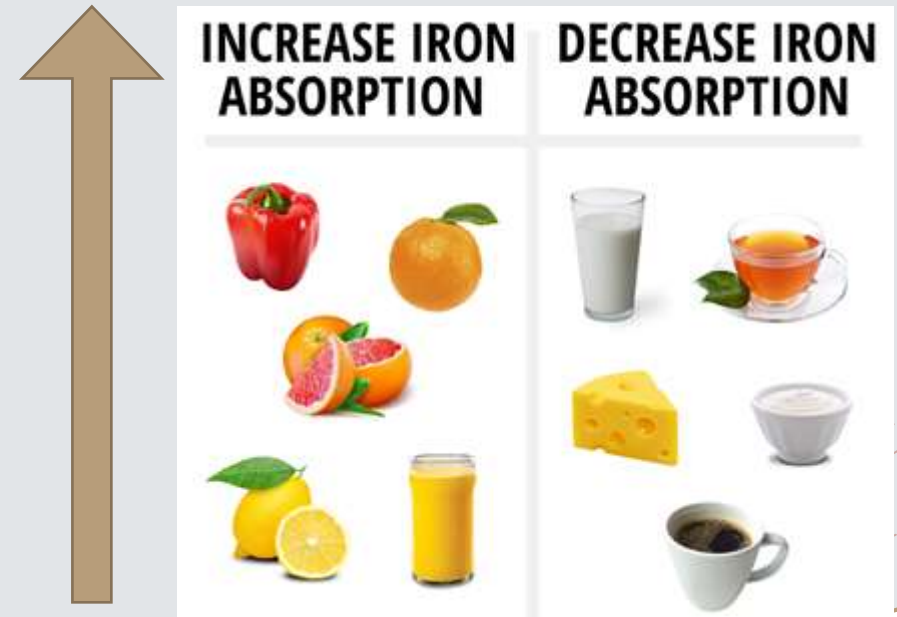
+ 1-2 mg/day



# Dietary absorption of iron

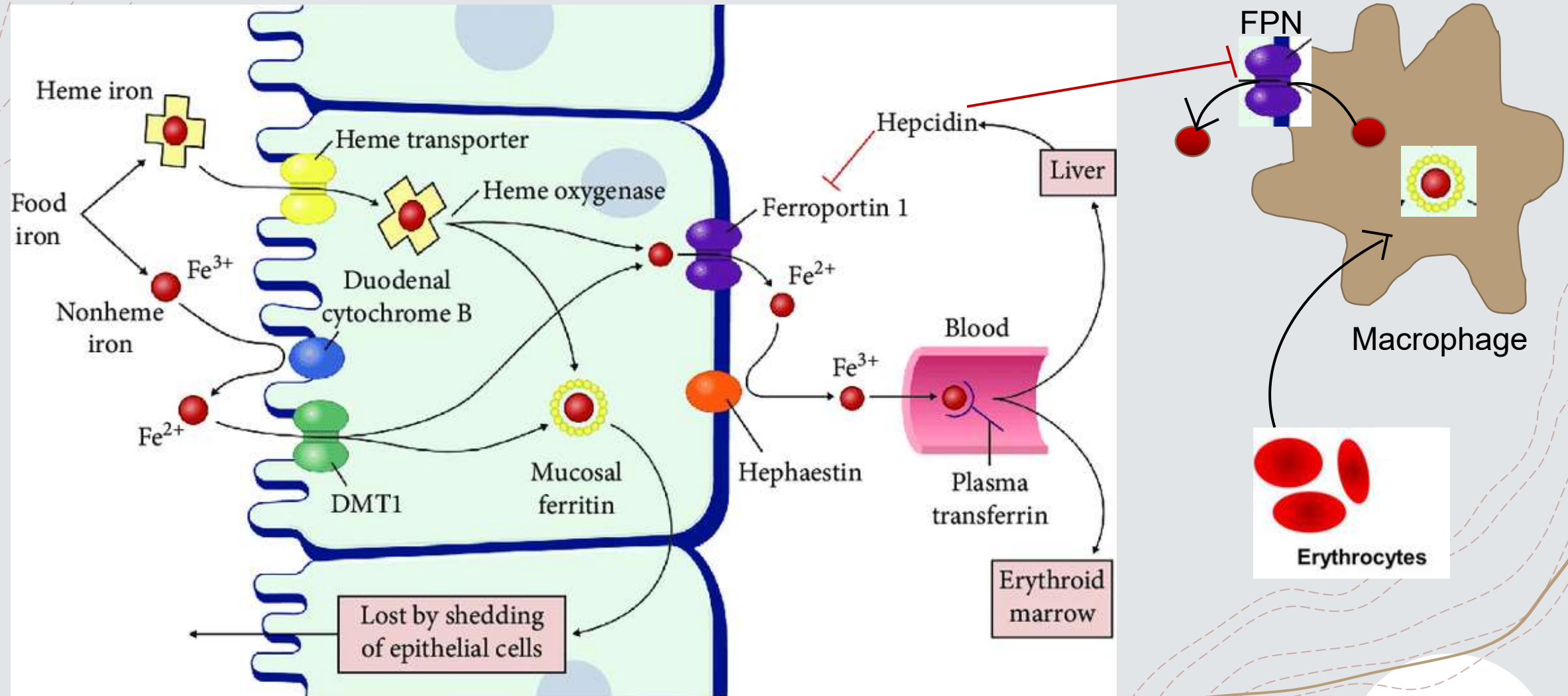


- + inorganic (non-haem) (90%)
- + haem-bound
- + incorporated within ferritin (min)





# Iron absorption, transport & storage



# Regulation of iron homeostasis



CELLULAR:  
**IRON REGULATORY  
PROTEINS (IRP)**

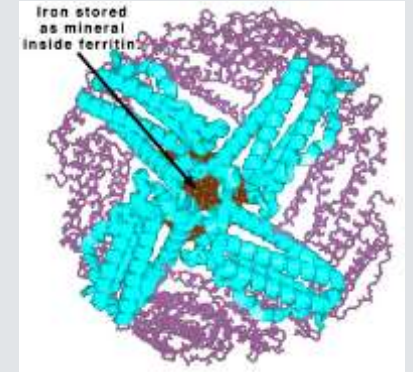


SYSTEMIC:  
**HEPCIDIN**

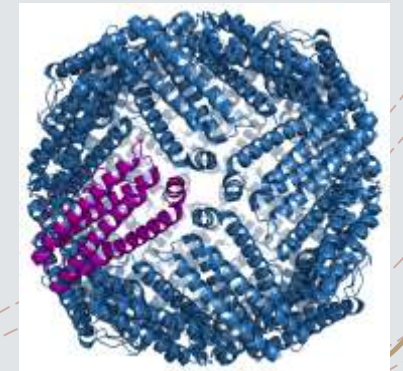
# Cellular iron homeostasis



- Limiting further iron influx



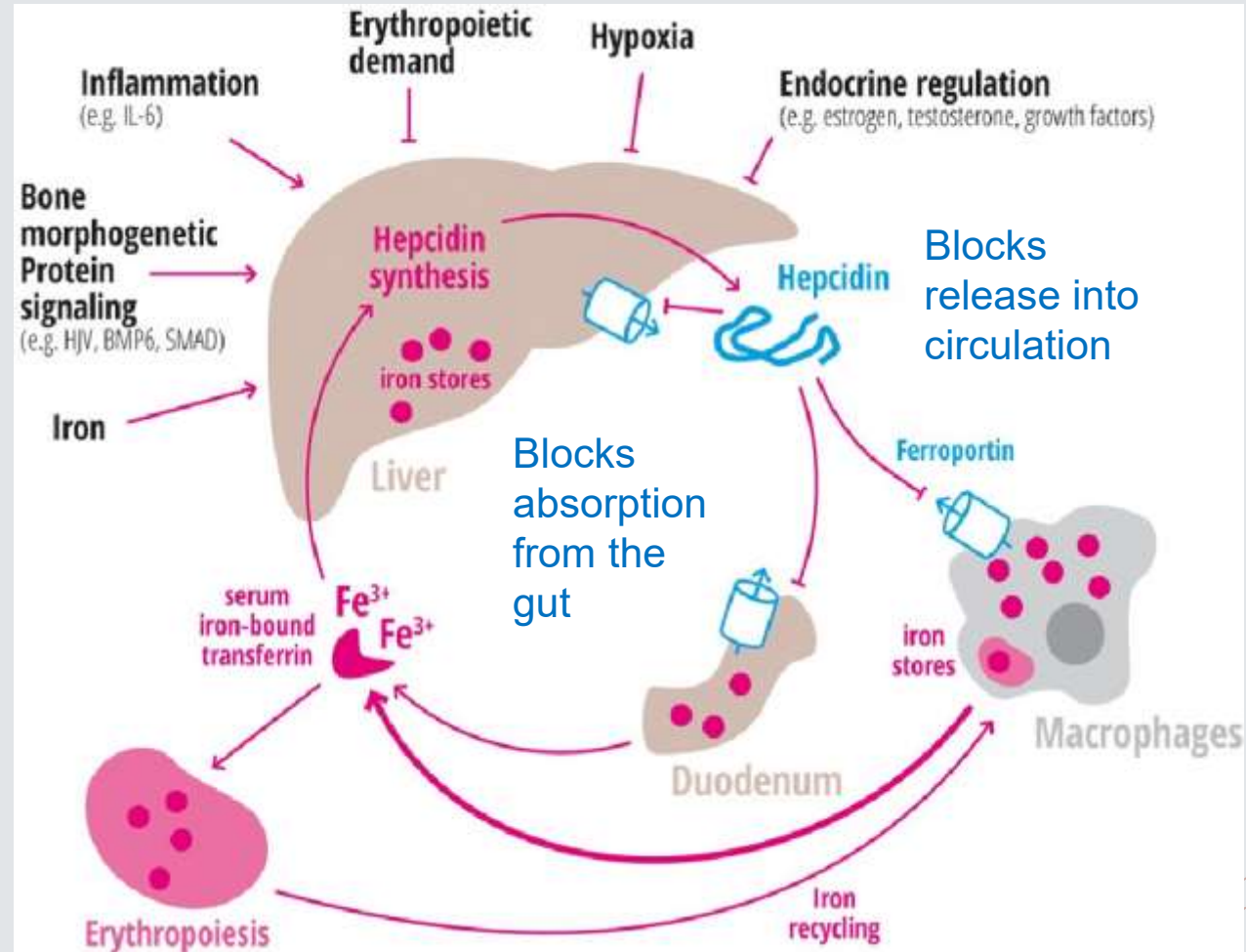
- Allowing further iron influx



# Systemic iron homeostasis

## ↑ Hepcidin

- + ↑ iron stores
- + malignancy
- + Infection
- + Inflammation



## ↓ Hepcidin:

- + ↓ iron stores
- + anaemia
- + hypoxia
- + erythropoietic demand

# Must get the balance right!



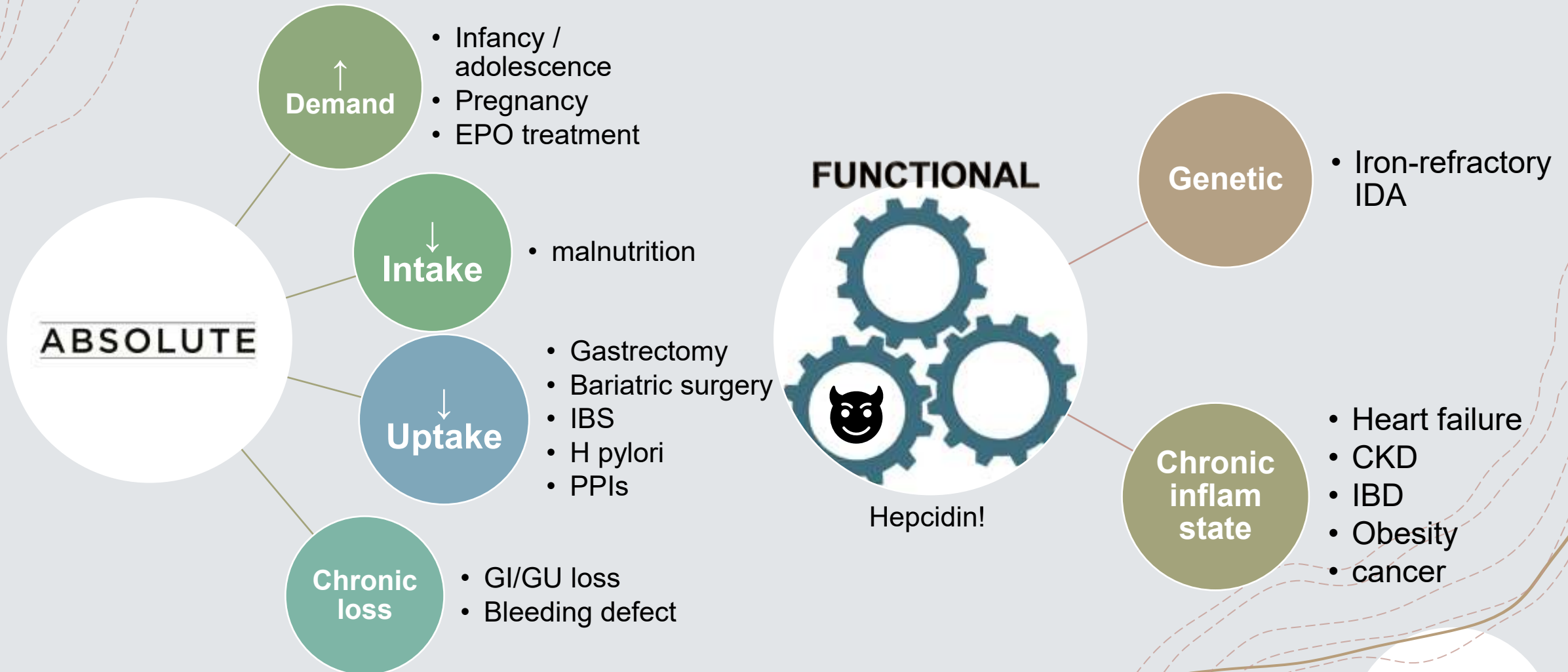
Iron overload

Free iron catalyses formation of ROS  
→ damages cellular structures  
→ dysfunction, apoptosis, necrosis in liver, heart & endocrine system

- fatigue, lethargy, dyspnoea
- myocardial dysfunction
- impaired neonatal brain development
- immune dysfunction
- impaired DNA repair & replication
- impaired thyroid function

Iron deficiency

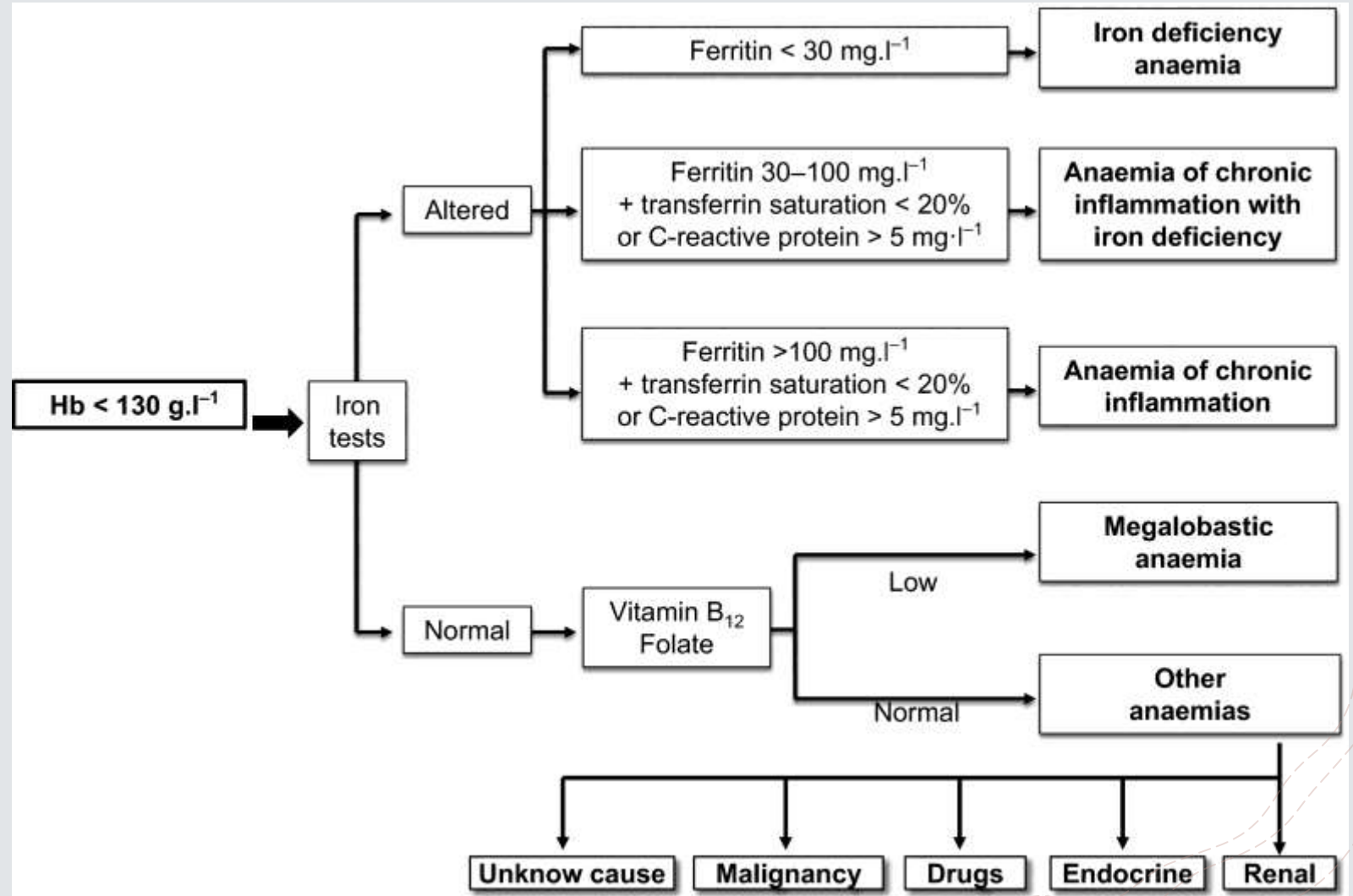
# Causes of iron deficiency (ID)



# Investigations for iron deficiency

Test	Reflects	Normal	Iron restriction
Serum ferritin ( <b>SF</b> )	Iron stores	30 – 300 µg/l	<30 µg/l = low stores ≤12 µg/l = iron restriction
Transferrin saturation ( <b>Tsat%</b> )	Iron mobilisation (functional ID / iron sequestration)	20 – 50%	<16% <20% if CKD
Mean corpuscular volume ( <b>MCV</b> )	Issue with either globin or iron restriction	80 – 100 fl	<80 fl
Red cell markers e.g. <b>MCHr</b>	How iron is being used by the bone marrow	MCH 27.0 – 32.0 pg (of Hb/RBC)	MCHr <27.6 pg

# Classification of perioperative anaemia





# Treatment for iron deficiency anaemia

- + Establish the cause & correct
- + If sufficient time (>6 weeks) → oral iron & nutritional advice
- + 40 – 60mg elemental iron daily / 80 – 100mg alternate days
- + Oral iron is cheap but longer treatment & more side effects (GI)
- + Re-check Hb in 4 weeks for response
- + Once IDA corrected, continue 3 months to rebuild stores



# Oral iron

**Table 2.** Recommended daily dose and elemental iron content of oral iron preparations.

Iron salt	Preparation	Elemental iron content
Ferrous fumarate	210 mg	65 mg
Ferrous gluconate	300 mg	35 mg
Ferrous sulphate (dried)	200 mg	65 mg
Ferrous feredetate	190 mg/5 ml elixir	27.5 mg/5 ml elixir

# Intravenous iron

## Indications

- Oral iron poorly tolerated
- Oral iron ineffective
- Time to surgery <6 weeks
- Functional iron deficiency

## Contraindications

- Iron overload
- Disorders of iron utilisation
- Known hypersensitivity
- 1<sup>st</sup> trimester of pregnancy

## Preparations

- Total dose:
  - Sugars: Ferinject, Monofer
  - Dextrans: Cosmofer
- Low-dose: Venofer
- Dose: 1000-1500mg slow ivi <1h

## Adverse effects

- Hypersensitivity
- skin staining with extravasation
- hypophosphataemia

# Treatment algorithm for pre-operative anaemia

## Investigations:

## Management:

### PO iron if:

- >6 weeks

### IV iron if:

- <6 weeks / timing critical
- Inadequate response to PO
- Poor tolerance
- Non-compliance
- Impaired GI absorption
- Haemodialysis
- Anaemia of chronic inflammation ± iron deficiency

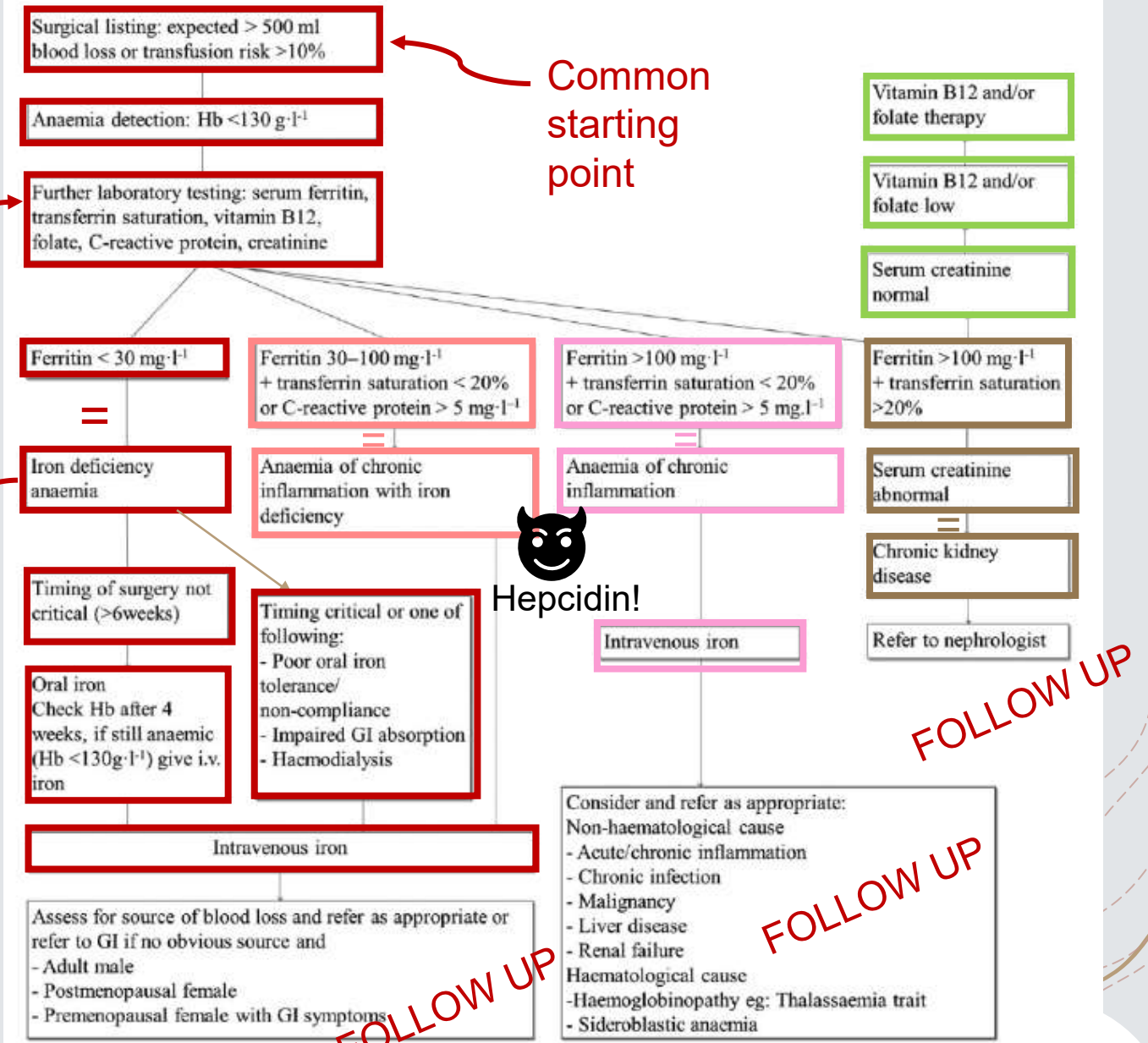


Figure 1 Treatment algorithm for pre-operative anaemia.

# ID in obstetrics – the problem

- + Anaemia is common (38% worldwide in 2011)
- + Iron deficiency is the main cause
- + Pregnancy requires + 1g iron
- + Breastfeeding requires + 1mg iron /day
- + → Deficit would take 2 years to repay with dietary iron!



# ID in obstetrics – the consequences

## Anaemia =

- 1<sup>st</sup> trimester: Hb <110 g/l
- 2<sup>nd</sup>-3<sup>rd</sup> trimester: Hb <105 g/l
- Postpartum: Hb <100 g/l

↓  
Serum ferritin < 30 µg/l  
MCH <27 pg

## Maternal

↑ risk death

↑ infection risk

Uterine atony

APH & PPH

## Fetal

Low birth weight

Fetal anaemia

Preterm & perinatal mortality

Caesarean section

Unplanned NICU

# ID in obstetrics – the solution

## Oral iron

- ✓ micro-/normocytic anaemia  
@28/40
- ✓ elemental iron 40-80mg OM
- ✓ re-check Hb in 2-3 weeks
- ✓ check SF routinely in high-risk patients or if Hb doesn't increase with oral iron

## IV iron

- ✓ no response to oral iron
- ✓ oral iron not tolerated
- ✓ Surgery planned <6 weeks
- ✓ EI CS + Hb <105g/l / SF <30µg/l
- ✓ EBL >20% blood volume (90-100 ml/kg booking weight)
- ✓ E.g. Ferinject

# Methods of reducing transfusion requirement



PREOP	INTRAOP	POSTOP
Oral iron	Cell salvage	Accept lower transfusion threshold
IV iron	Meticulous surgical technique	Further iron supplementation
Treat underlying chronic disease	Balanced physiology (avoid hypothermia, acidosis, hypocalcaemia)	Reduce frequency & volume of blood sampling (paed /reduced fill bottles)
Recombinant erythropoietin	Topical haemostatic agents	Minimise drains
Folic acid & vitamin B12	Neuraxial block	
Discontinue antiplatelets	Tranexamic acid	
	POC testing (TEG/ROTEM)	
	Consider controlled hypotension	



# Summary

- +40% of major surgical patients
- + Perioperative anaemia → increased complications
- + Physiological effects of anaemia & blood loss
- + Commonest cause of anaemia is iron deficiency
- + Iron homeostasis is important
- + Hepcidin controls iron absorption and movement into circulation
- + Treatment starts with determining the cause
- + Iron supplementation – oral and intravenous
- + IDA is common in obstetrics and should be appropriately managed

# References

- + “Iron homeostasis and perioperative management of iron deficiency”, BJA Education, 19(12): 390-397 (2019)
- + “International consensus statement on the perioperative management of anaemia and iron deficiency”, Anaesthesia 2017, 72, 233-247 Consensus Statement
- + “Addressing preoperative anaemia”, PQIP (Perioperative Quality Improvement Programme)
- + “Optimisation of pre-operative anaemia in patients before elective major surgery – why, who, when, how?”, Anaesthesia 2019, 74(Suppl. 1), 49-57
- + NICE 2018 summary ‘Anaemia - iron deficiency: <https://cks.nice.org.uk/topics/anaemia-iron-deficiency/>
- + Obstetric Anaesthetists Handbook, thirteenth edition, February 2020
- + **UK guidelines on the management of iron deficiency in pregnancy**, British Journal of Haematology, vol 188, issue 6, pages 819 – 830, March 2020