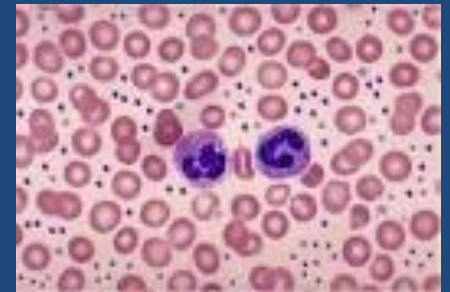




East Suffolk and North Essex
NHS Foundation Trust

Current thinking in Haematology – Iron, Paraproteins and VITT



17/06/21

Andrew Hodson
Consultant Haematologist
Ipswich Hospital

Aims

- Discuss common and relevant issues
- Primary care focus
 - RCGP curriculum
- Who, when and to whom to refer?
- Feedback

Themes

- Anaemia
 - Iron deficiency
- Paraproteins
 - Is it Myeloma?
 - How do I interpret serum free light chains?
 - What do I do with MGUS?
- VITT

Normal FBCs

Hb	157	g/L	(135 - 175)
WBC	6.9	$\times 10^9/L$	(4.0 - 11.0)
Plt	262	$\times 10^9/L$	(135 - 450)
RBC	5.44	$\times 10^{12}/L$	(4.50 - 5.50)
MCV	83	fL	(80 - 100)
HcT	0.45	L/L	(0.38 - 0.50)
MCH	28.9	pg	(27 - 34)
MCHC	348	g/L	(300 - 360)
RDW	12.6		(10 - 15)
Neutrophils Ab's	4.6	$\times 10^9/L$	(2.0 - 7.5)
Lymphocytes Ab's	1.7	$\times 10^9/L$	(1.0 - 4.0)
Monocytes Ab's	0.5	$\times 10^9/L$	(0.1 - 1.0)
Eosinophils Ab's	0.1	$\times 10^9/L$	(0.0 - 0.5)
Basophils Ab's	0.0	$\times 10^9/L$	(0 - 0.2)

Normal FBCs

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Basophils Ab's	0.0	$\times 10^9/L$	(0 - 0.2)

Normal FBCs

- Ranges are specific to
 - Laboratory
 - Ethnicity
 - Age
 - Sex
- Determined from local healthy population ideally
- In practice UK textbook reference ranges often used

Anaemia

- Rate of decline
 - days/weeks/months/years
- Transfusion thresholds
- How is the patient?
- Are the other blood counts low?
- What is the MCV?

MCV

- First thing everyone should look at
- Low (<80fl)
 - Iron deficiency until proven otherwise
 - Thalassaemia
 - Lead poisoning (fishing weights factory in Ipswich)

MCV

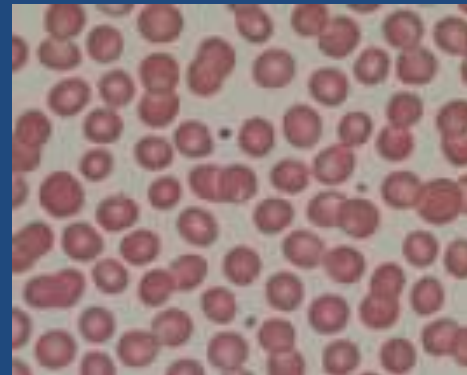
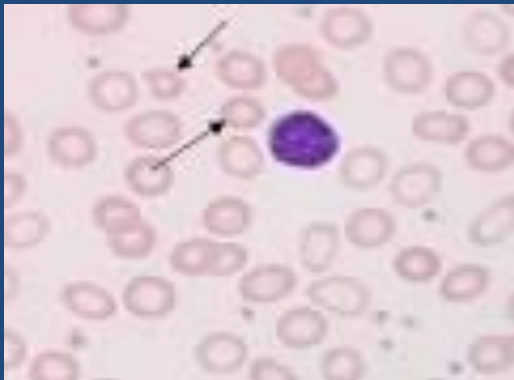
- Very helpful for classifying anaemias

- Low (<80fl)

Iron deficiency if new and until proven otherwise

Thalassaemia – will always have been the same

Lead poisoning



Case 1

- 30 year old female
- Presents to GP with gradual onset of fatigue and shortness of breath on exertion
- Looks pale
- FBC checked

Case 1

- Hb 80g/L
 - MCV 70fl
 - WCC $5.4 \times 10^9/L$
 - Platelets $480 \times 10^9/L$
 - White cell differential normal
-
- What is the problem?
 - What is the likely diagnosis?
 - What tests would confirm this?
 - What further information would be useful?
 - Would you plan any further tests?

Case 1

- What is the problem?
 - Microcytic anaemia
- What is the likely diagnosis?
 - Iron deficiency
- What tests would confirm this?
 - Ferritin (iron storage protein)
- What further information would be useful?
 - Possible causes
 - menorrhagia
 - dietary deficiency
 - gastrointestinal loss
- Would you plan any further tests?

Iron deficiency

- Most common cause of anaemia worldwide
 - 1.2 billion people affected
 - Prevalence
 - 42% in children
 - 29% in non-pregnant women
 - 38% in pregnant women
- Iron deficiency without anaemia (IDWA)
 - Likely twice as common
- It is not a haematological disease!

Iron deficiency

- Most common cause of anaemia worldwide
 - 1.2 billion people affected
- Iron deficiency without anaemia (IDWA)

Red cell haematology

This includes sickle cell disease, thalassaemia, aplastic anaemia and haemolytic anaemia. To the surprise of many, haematologists do not (or at least should not) have clinics full of patients with iron deficiency anaemia as this is really a gastroenterology or gynaecology problem. In addition to addressing the treatment of the conditions themselves (which involves careful initiation of transfusion programmes, powerful immunosuppressant drugs and sometimes stem cell transplantation), careful attention has to be paid to the complications of treatment such as iron overload.

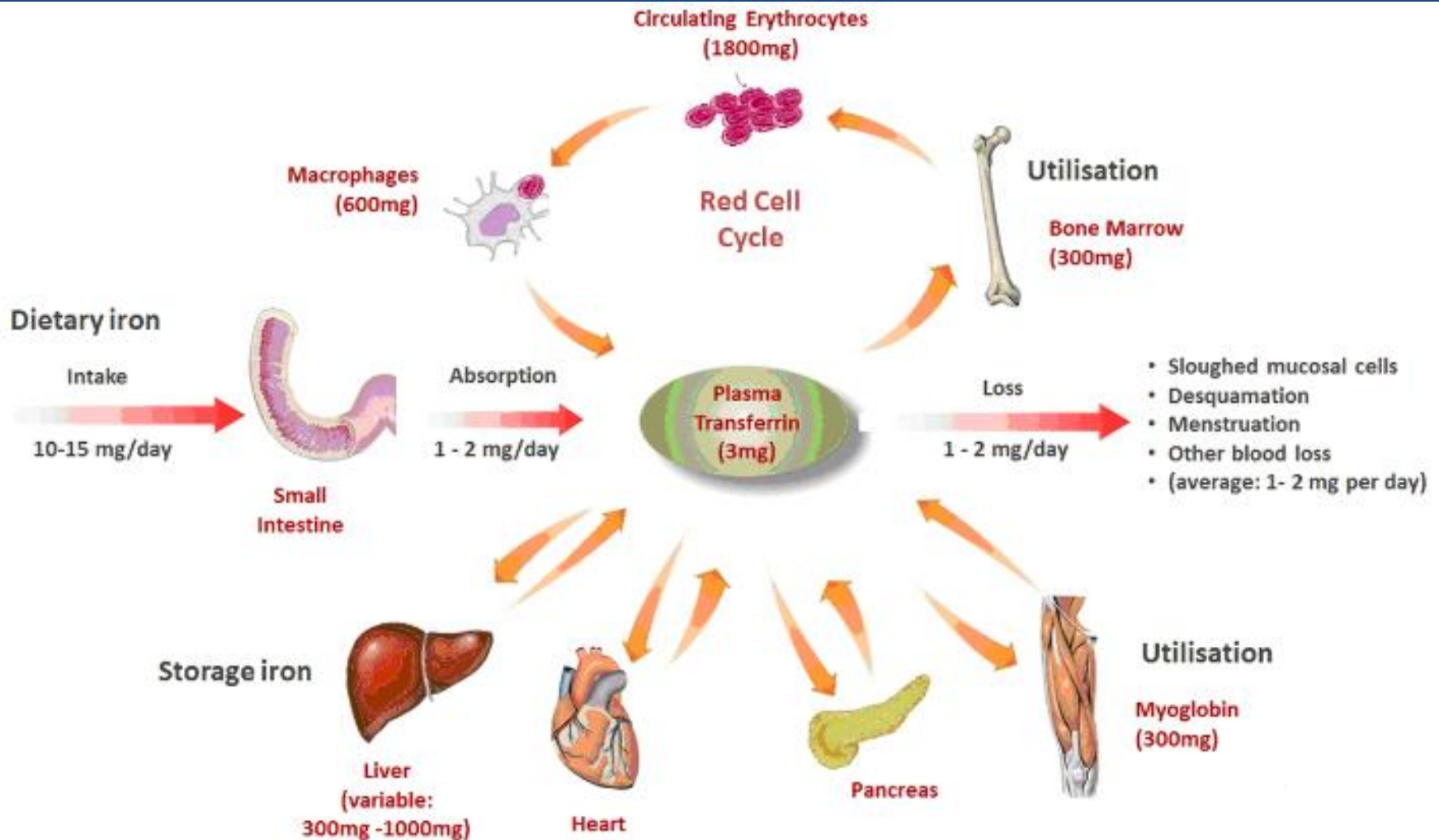
Iron deficiency

- Most common cause of anaemia worldwide
 - 1.2 billion people affected
- Iron deficiency without anaemia (IDWA)
 - Twice as common
- It is not a haematological disease!
- Most prevalent nutritional deficiency
- Symptoms may occur before anaemia

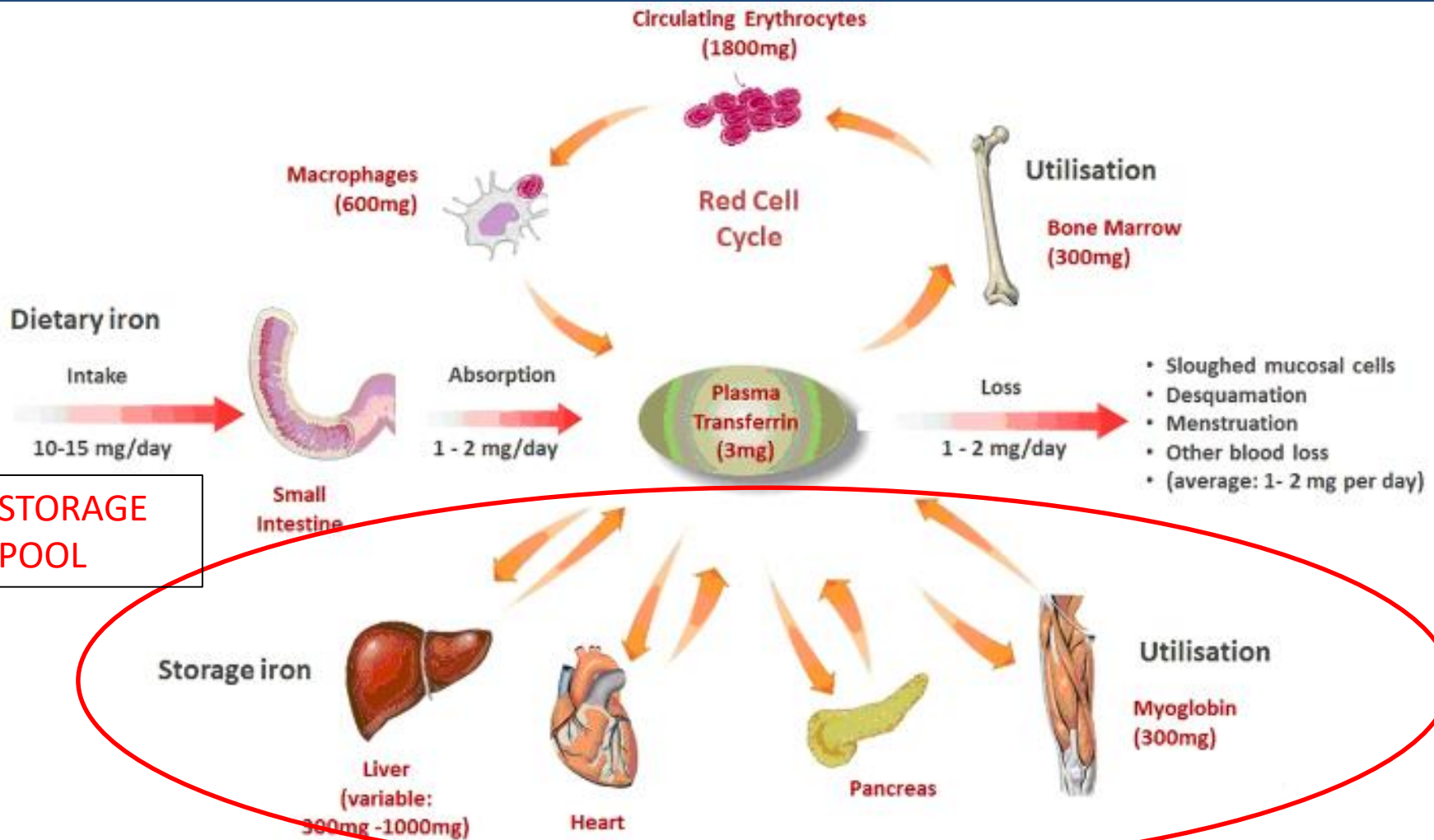
Iron deficiency without anaemia (IDWA)

- Distinct from IDA as not anaemic
- However a normal Hb for one person may be low for another (ie usual Hb higher)
- Important to recognise
 - Associated with fatigue
 - Worse outcomes in heart failure

Iron cycle

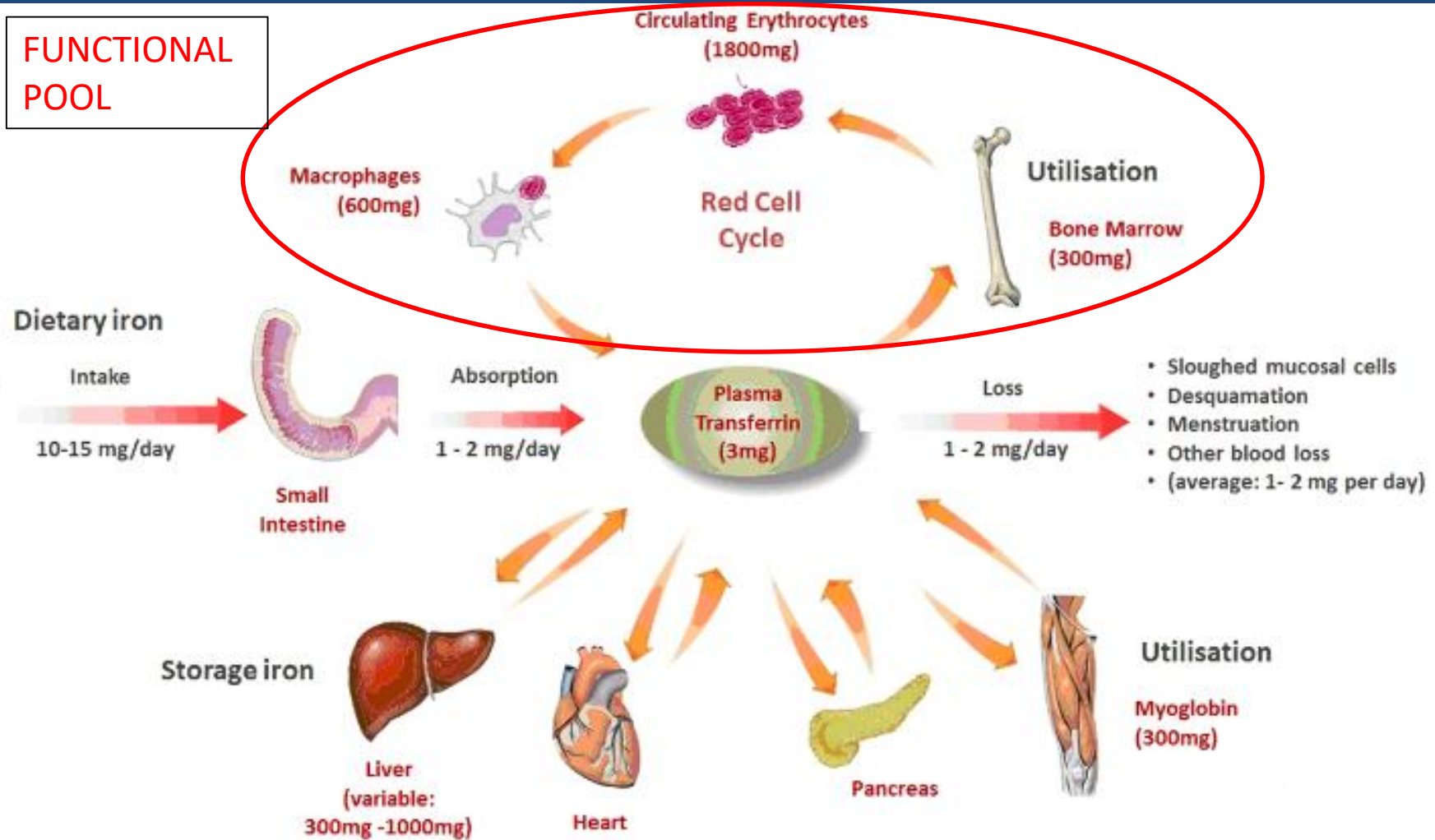


Iron cycle



Iron cycle

FUNCTIONAL POOL



Iron deficiency

- Occurs due to
 - Reduced dietary intake
 - Inadequate iron absorption
 - Increased iron utilisation
 - Iron (blood) loss
 - Chronic inflammation

Causes

- Reduced dietary intake
 - Vegetarian/Vegan diets
 - Malnutrition
- Increased utilisation
 - Pregnancy
 - Children
 - EPO treatment (ESRF)
 - Elite athletes

Causes

- Reduced absorption
 - Gastric acid (GA) required for conversion of Fe^{3+} to Fe^{2+} (better absorbed)
 - Bariatric surgery reduced surface area and acid
 - H Pylori reduces iron absorption +/- bleeding
 - Autoimmune gastritis reduces GA
 - PPI/H2 receptor antagonists reduce GA
 - Coffee/tea/Calcium (supplements or dairy)

Causes

- Chronic blood loss
 - GI cancers
 - Blood donation
 - Menorrhagia
 - Nosebleeds
 - Haematuria
 - Surgery/trauma
 - Infections eg hookworm
 - Angiodysplasia
- Chronic blood loss
 - NSAIDS/Steroids
 - Anticoagulants
 - Antiplatelets

Causes

- Chronic inflammation
 - Coeliac disease/IBD/RA/Malignancy
 - Increased hepcidin production
 - Blocks iron absorption
 - Causes entrapment in the reticuloendothelial system
 - Functional iron deficiency

CNS

Headache

Absentmindedness

↓ Cognitive function

Fatigue

Depression

Sleep disturbance

Impaired memory

Cardiorespiratory

Palpitations

↓ Exercise tolerance

Shortness of breath

Muscles and connective tissue

Muscle and joint pain

Dry skin

Weakness

Restless legs

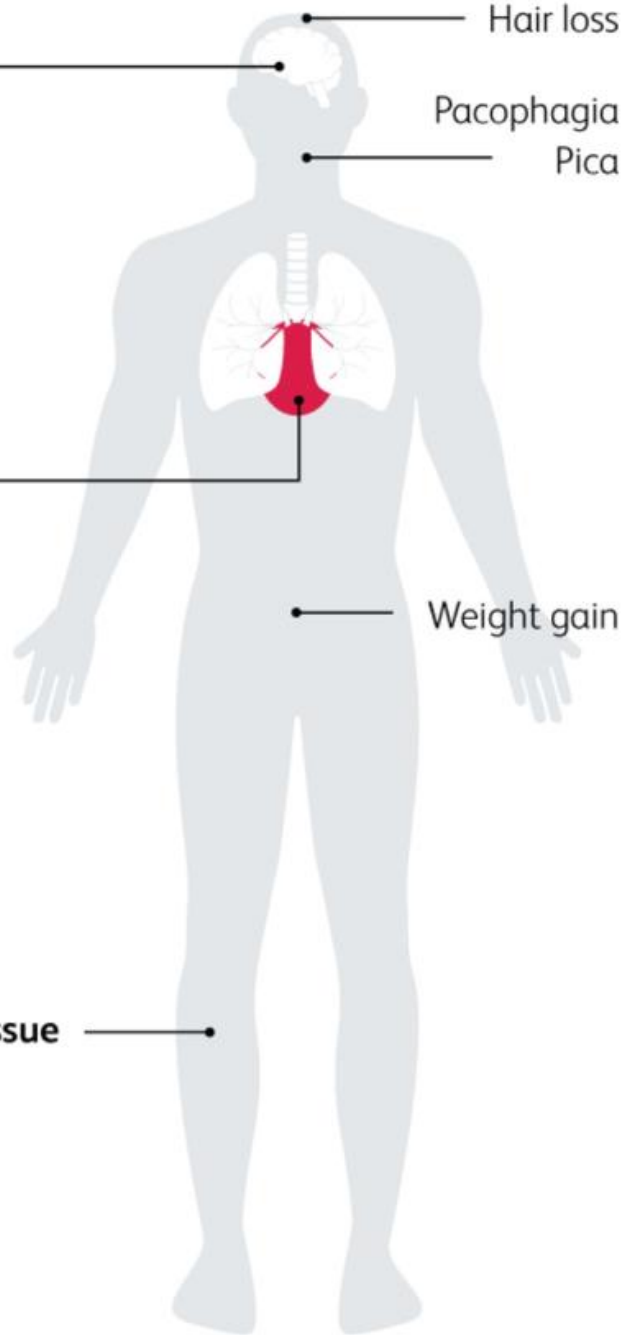
↓ Exercise tolerance

Hair loss

Pacophagia

Pica

Weight gain



CNS

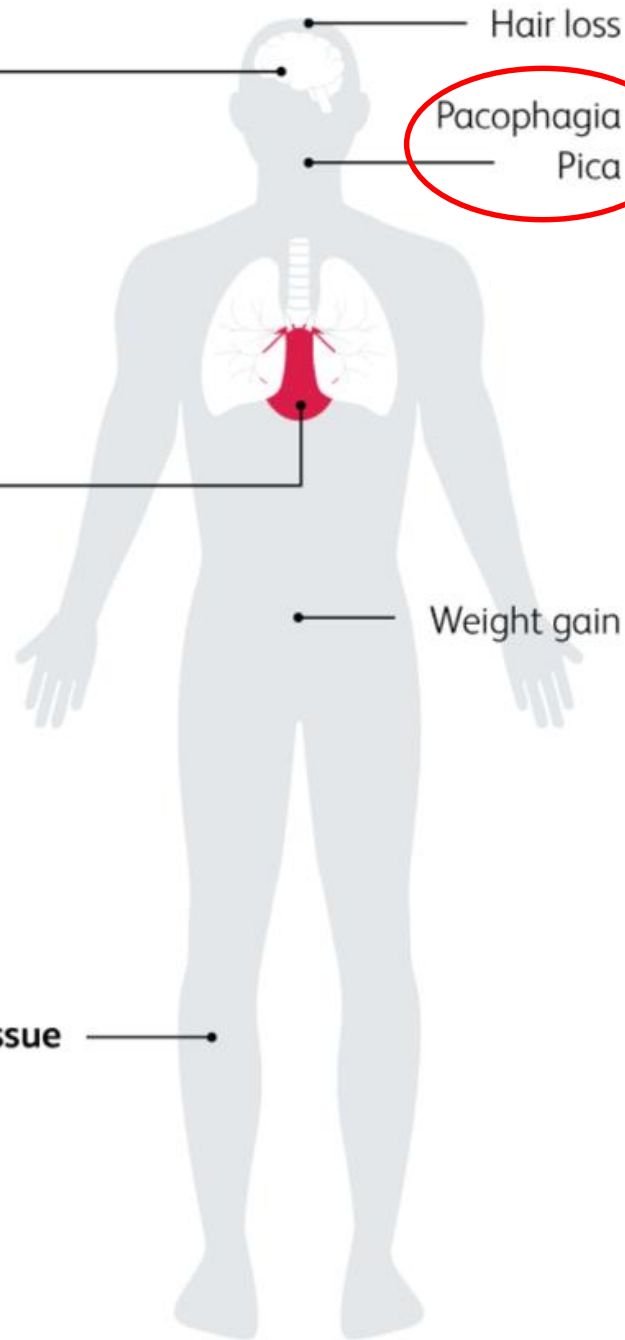
- Headache
- Absentmindedness
- ↓ Cognitive function
- Fatigue
- Depression
- Sleep disturbance
- Impaired memory

Cardiorespiratory

- Palpitations
- ↓ Exercise tolerance
- Shortness of breath

Muscles and connective tissue

- Muscle and joint pain
- Dry skin
- Weakness
- Restless legs
- ↓ Exercise tolerance



Persistent eating of ice, freezer frost or iced drinks for at least 1 month.

Iron deficiency

History

- Diet
- History of overt bleeding
 - GI/GU
 - Don't forget
 - menstrual history
 - BLOOD donors
 - Venesection patients (haemochromatosis)
- Drug history
 - NSAIDS
 - Corticosteroids
 - Aspirin/Clopidogrel
 - SSRIs

Iron deficiency History

- Travel history
 - Hookworm
- Related symptoms
 - Angina/palpitations
 - SOB/OE
 - Ankle swelling
- Weight loss

Iron deficiency anaemia

- Clinical features

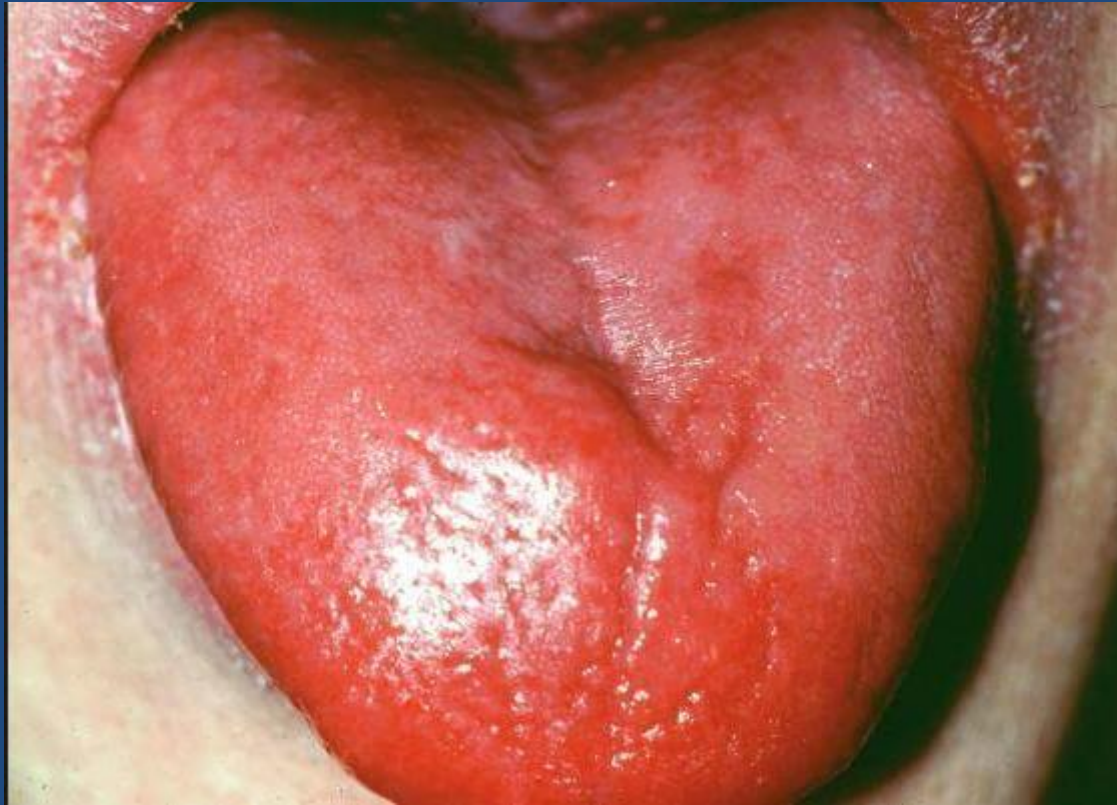


Iron deficiency anaemia

- Cl



Iron deficiency anaemia



Investigation

- FBC
- MCV <95
 - 97.6% sensitive for iron deficiency
- Blood film comments
 - Hypochromasia = pale red cells
 - Microcytosis = small red cells
 - Polychromasia = new red cells (reticulocytes)

Investigation

- Check ferritin
 - WHO defines low ferritin as
 - <15ng/ml adults
 - <12ng/ml children
 - In clinical practice iron deficiency is found at levels <30ng/ml
 - Normal ranges
 - Males/post menopausal females 30-400ng/ml
 - Females aged 20-60 – 13-150ng/ml

Investigation

- Raised in inflammation/malignancy/liver disease
 - Check CRP/LFTs
 - Ferritin $<100\text{ng/ml}$ = iron deficient in states of chronic inflammation
 - Role for iron studies

Iron studies

- Ferritin
 - Acute phase protein so raised in infection/inflammation
- Serum iron
 - Tend to be low but fluctuate and not reliable
- Transferrin
 - Often raised in ID
- Transferrin saturation
 - <20% diagnostic of ID
 - Useful when ferritin measures 100-300ng/ml in chronic inflammation but ID suspected

Iron studies

Serum Iron	11.7	umol/L	(6.6 - 26)
Transferrin	2.32	g/L	(2.0 - 3.6)
Saturated Transferrin	22	%	(15 - 50)
Ferritin	233	ng/ml	

NORMAL

Serum Iron	7.1	umol/L	(6.6 - 26)
Transferrin	3.36	g/L	(2.0 - 3.6)
Saturated Transferrin	9	%	A (15 - 50)
Ferritin	15	ng/ml	

IRON DEFICIENT

Female Ferritin Reference Range
17-60 years: 13-150 ng/mL

Ferritin ranges are age and sex specific

Investigation

- Young females
 - Ask about periods – length and how heavy
 - Consider bleeding disorders eg ITP / von Willebrands disease
- Men and post-menopausal females (>60)
 - Examine
 - Endoscopy (upper and lower GI)
 - TTG test – coeliac disease (often folate deficient aswell)
 - Ova cysts and parasites in stool
 - Urine – blood
 - Iatrogenic – venesections for haemochromatosis

Referral

- 2WW for IDA to lower GI pathway
 - Aged >60 (Refer)
 - Aged <50 with PR bleeding (Consider)
 - FIT testing
 - Aged <60 with IDA
 - Aged >60 with anaemia (incl without ID)
 - Premenopausal females
 - Colonic symptoms
 - Strong FH (2+ 1st degree relatives or 1 if <50)
 - Persistent IDA despite treatment

Referral

- Gynaecology
 - Menorrhagia not responding to medical therapy
 - Post menopausal
 - Age >55 2WW
 - Age <55 consider 2WW
 - Pregnant
 - Severe anaemia / symptoms
 - Late gestation (>34 weeks)
 - No response to oral iron

Treatment

- Diagnostic trial of oral iron
 - Pregnant women
 - Premenopausal females with menorrhagia
 - In known haemoglobinopathy check ferritin first
 - Do not use in men or post-menopausal females

Treatment

- Dietary advice
 - Meat/poultry/fish 5 x week
 - Wholemeal products
 - Legumes
 - Vegetables

- Consider referral to a dietician for advice

Treatment

- Iron replacement
 - NICE CKS – elemental iron 65mg 3x daily
 - Equates to Ferrous Sulphate 200mg TDS
 - Ferrous gluconate 300mg – 35mg elemental iron
 - Ferrous fumarate 300mg – 99mg elemental iron
 - Commonly associated with
 - Constipation/diarrhoea
 - Dyspepsia/nausea
 - Poor adherence

Treatment

- Single dose alternate days v multiple doses on consecutive days
 - Higher cumulative iron absorption
 - Lower hepcidin levels (more efficient iron absorption)

- Stoffel et al, Lancet Haematol 2017;4:e524-33

Iron deficiency anaemia

THE LANCET
Haematology



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Articles


Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice-daily split dosing in iron-depleted women: two open-label, randomised controlled trials


Nicole U Stoffel, MSc, Colin I Cercamondi, PhD, Prof Gary Brittenham, MD, Christophe Zeder, MSc, Anneke J Geurts-Moespot, BSc, Prof Dorine W Swinkels, PhD, Diego Moretti, PhD[†], Prof Michael B Zimmermann, MD[†]  

[†] Senior authors

Published: 09 October 2017

 PlumX Metrics 

DOI: [http://dx.doi.org/10.1016/S2352-3026\(17\)30182-5](http://dx.doi.org/10.1016/S2352-3026(17)30182-5) |  CrossMark



Treatment

- Elemental iron 35-50mg daily or 100mg alternate days (ASH/BSG guidelines)
 - Ferrous sulphate 200mg OD or 200mg BD alt days
 - = 65mg elemental iron per tablet
 - Ferrous gluconate 300mg OD or 300mg 2-3 tablets alt days
 - = 35mg elemental iron per tablet
 - Ferrous fumarate 300mg OD alternate days (generally avoid due to concentrated dose elemental iron)
 - = 99mg elemental iron

Treatment

- Take between meals
- Avoid inhibitors of absorption (dairy, tea, coffee)
- Avoid antacids / PPI co-administration
- Vitamin C (Ascorbic acid or orange juice) enhances absorption

Treatment

- Check tolerance at 1 week
- Repeat FBC/ferritin at 6-8 weeks
 - Aim ferritin >100ng/ml
- Reticulocytosis starts in 4-5 days
- Hb begins to improve by week 2
- Take for 3-6 months
- Better – repeat FBC/ferritin every 6-12 months
- Not better – IV iron

Treatment

- Role of parenteral iron
 - If oral iron ineffective or poorly tolerated
 - After gastric bypass
 - 1% minor infusion reactions
 - Severe reactions overstated as new preparations safer
 - Risk 1:250,000
 - Nevertheless should be given in a setting where adverse effects can be managed

Treatment

- Oral v IV iron
 - Oral cheaper and more freely available
 - Appropriate in
 - healthy patients
 - Minor-asymptomatic ID/IDA
 - Adherence is poor
 - Reduced efficacy over IV iron
 - IV iron is more limited in the UK than US

Treatment

- Role of blood transfusion
 - If cardiovascular compromise or debilitating symptoms
 - USA – ‘Choosing Wisely’ campaign for restrictive blood transfusion
 - Most cases are chronic and unlikely to need transfusion **irrespective of Hb level**

Iron deficiency in pregnancy

- In pregnancy ferritin falls to 50% of conception value due to haemodilution and utilisation
- ID leads to
 - Lower birth weight
 - Mental illness/impaired neurocognitive functions
- Check Hb at booking + 28 weeks
- Critical from week 32
- Oral iron alternate days in 1st trimester
- IV iron safe in 2nd/3rd trimesters if ID persists

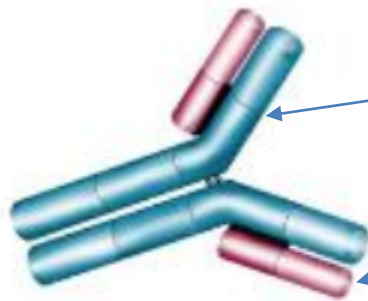
Iron deficiency references

- NICE CKS Anaemia – Iron deficiency
 - [//cks.nice.org.uk/topics/anaemia-iron-deficiency/](https://cks.nice.org.uk/topics/anaemia-iron-deficiency/)
- Management of iron deficiency. American Society of Haematology Education Program. 2019(1):315-322



Immunoglobulins

Monoclonal proteins can refer to: Intact Immunoglobulins (Igs)



Heavy chain –
IgG/A/M/D/E

Light chain
Kappa or Lambda

and/or free light chains (FLCs)



Immunoglobulins

- IgG, IgA, IgM (IgD/IgE)
- Commonest reason for elevation is infection or inflammation
- Protein electrophoresis will indicate raised gamma globulins with no monoclonal protein
- This is NOT myeloma
- Consider
 - Infections eg HIV
 - Inflammatory states
 - Malignancy
 - Liver disease
 - IgA often elevated in the elderly

Monoclonal proteins (Paraproteins)

- Abnormal monoclonal (M) protein produced by plasma cells
- Will be IgG / IgA / IgM based
- Should not be detectable
- When to test?
 - Hypercalcaemia*
 - Renal failure*
 - Anaemia*
 - Neuropathy
 - Bone pains
 - Elevated total protein or ESR
 - Suspicious bone lesions on imaging

Paraproteins

- Abnormal monoclonal protein produced by plasma cells
- Should not be detectable
- When to test?
 - Hypercalcaemia*
 - Renal failure*
 - Anaemia*
 - Neuropathy
 - Bone pains
 - Elevated total protein or ESR
 - Suspicious bone lesions on imaging

*Unexplained ie normal ferritin/B12/Folate, no other cause of renal failure

Could it be myeloma?

- What to request?
 - FBC + ESR
 - U+E
 - Bone screen

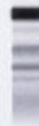
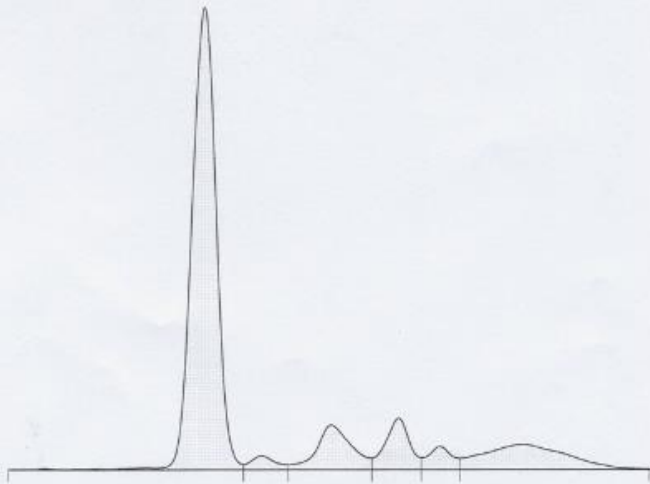
 - Immunoglobulins
 - Protein electrophoresis
 - Serum free light chains

NICE Guidance

- NG 12 Suspected cancer: recognition and referral
 - Myeloma
 - Offer FBC, calcium, ESR in people aged >60 with persistent bony pain, esp back pain, or unexplained fracture
 - Offer very urgent PE and BJP (sFLC) within 48 hours in people aged >60 with hypercalcaemia or leucopenia and a presentation that is consistent with possible myeloma
 - Offer very urgent PE and BJP (sFLC) if ESR/PV and presentation are consistent with possible myeloma
 - Refer via 2WW pathway if PE/BJP (sFLC) suggest myeloma

Protein electrophoresis

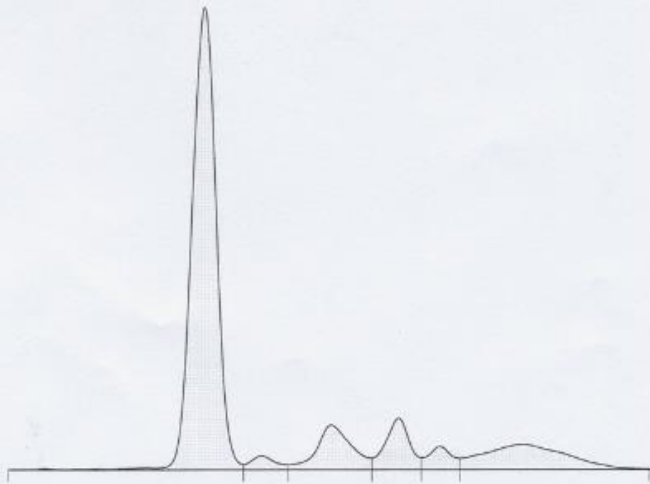
- Used in investigation of suspected
 - Myeloma
 - Lymphoma
 - Immunodeficiency
- Result may be
 - Normal
 - No abnormality noted
 - Abnormal
 - monoclonal protein
 - Polyclonal increase in gamma globulins (reactive)
 - Hypogammaglobulinaemia (immune deficiency)



Serum protein electrophoresis

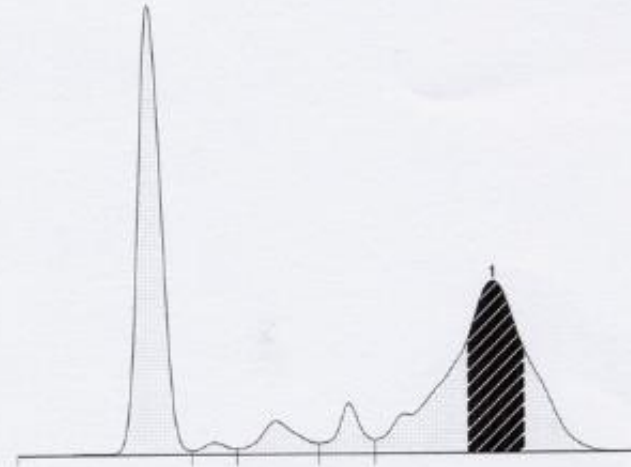
Fractions	%	Ref. %	Conc.	Ref. Conc.
Albumin	59.4 <	60.0 - 71.0	45.7	43.0 - 51.0
Alpha 1	2.4	1.4 - 2.7	1.8	1.0 - 2.0
Alpha 2	11.0	7.0 - 11.0	8.5	5.0 - 8.0
Beta 1	8.6	6.0 - 9.0	6.6	4.0 - 6.0
Beta 2	3.8	2.0 - 5.0	2.9	1.0 - 4.0
Gamma	14.8	8.0 - 16.0	11.4	6.0 - 12.0

NORMAL



Serum protein electrophoresis

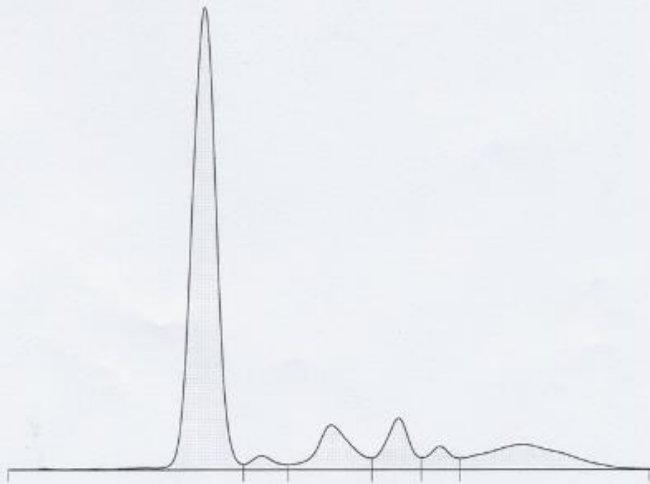
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Serum protein electrophoresis

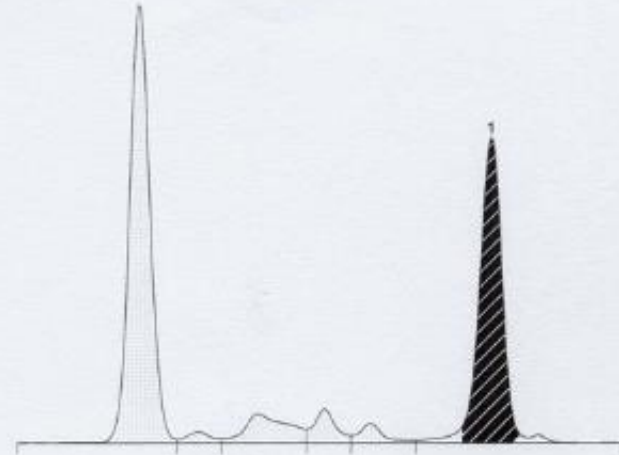
Fractions	%	Ref. %	Conc.	Ref. Conc.
Albumin	34.6 <	60.0 - 71.0	36.0	43.0 - 51.0
Alpha 1	1.2 <	1.4 - 2.9	1.2	1.0 - 2.0
Alpha 2	5.0 <	7.0 - 11.0	5.2	5.0 - 8.0
Beta	4.8 <	8.0 - 13.0	5.0	6.0 - 9.0
Gamma	54.4 >	9.0 - 16.0	56.6	6.0 - 11.0
1	28.6		29.7	

HYPERGAMMAGLOBULINAEMIA



Serum protein electrophoresis

Fractions	%	Ref. %	Conc.	Ref. Conc.
Albumin	59.4	60.0 - 71.0	45.7	43.0 - 51.0
Alpha 1	2.4	1.4 - 2.7	1.8	1.0 - 2.0
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Serum protein electrophoresis

Fractions	%	Ref. %	Conc.	Ref. Conc.
Albumin	43.2	60.0 - 71.0	39.3	43.0 - 51.0
Alpha 1	1.5	1.4 - 2.7	1.4	1.0 - 2.0
Alpha 2	7.3	7.0 - 11.0	6.6	5.0 - 8.0
Beta 1	4.3	6.0 - 9.0	3.9	4.0 - 6.0
Beta 2	2.7	2.0 - 5.0	2.5	1.0 - 4.0
Gamma	41.0	8.0 - 16.0	37.3	6.0 - 12.0
1	38.7		35.2	

MONOCLONAL PROTEIN

Paraprotein

- Increase in an identical (monoclonal) immunoglobulin
- Common causes
 - Monoclonal gammopathy of undetermined significance
 - Myeloma
 - Plasmacytoma
 - Lymphoma - usually low grade NHL
 - Amyloidosis

Serum free light chains

- Replace 24 hour urinary free light chain (Bence-jones) quantitation
- The ratio is key!
- Normal ratio – 0.26-1.65
- If eGFR <60ml/min normal is 0.37-3.1
- Normal sFLC ratio – not myeloma
- **Proportional** rises seen in renal failure
- Refer if <0.125 or >8 or single chain >500mg/L

MGUS

- Benign condition
- 2-4% of over 70s
- PP <30g/L, usually less than 15g/L
- sFLC ratio normal / mildly abnormal
- Use prognostic calculator (Mayo Clinic)
- Repeat at 4 months
- If stable 6 monthly for 2 years then annually if no change

MGUS

- Criteria for referral
 - IgG PP >15g/L
 - IgA/IgM >10g/L
 - sFLC ratio <0.125 or > 8
 - Individual light chain >500mg/L
 - Symptoms
 - Anaemia
 - Renal failure
 - Hypercalcaemia
 - Bone pains
 - Other cytopenias
 - B symptoms
 - Enlarged spleen / nodes

MGUS

MGUS prognosis

Risk stratification of monoclonal gammopathy of uncertain significance

1. Assess patient for each of three risk factors

- Abnormal serum free light chain ratio (SFLC)
- Serum M protein ≥ 15 g/L
- M protein not of IgG subtype

2. Sum the number of risk factors to determine risk category and prognosis

Number of factors	Risk category	20 year progression risk (%)	20 year progression risk accounting for death as competing factor (%)
0	Low	5	2
1	Low-intermediate	21	10
2	High-intermediate	37	18
3	High	58	27

Myeloma

- Malignant plasma cell disease
 - Monoclonal protein IgG or IgA
 - Anaemia
 - Renal failure
 - Hypercalcaemia
 - Bone disease / pain
- Treat with systemic anti-cancer therapy

Plasmacytoma

- Malignant plasma cells in one area
- Bone or soft tissue
- Pain/swelling/fracture
- Treat with radiotherapy

2WW referral criteria

- Results of PE or sFLC suggest myeloma
- PP >30g/L
- PP >15g/L (IgG) or 10g/L (IgA/IgM) with symptoms/results of concern
- sFLC ratio <0.125 or > 8
- Radiology suggestive of myeloma **and** myeloma screen supports this

Super urgent referrals

- Calcium >3
- AKI
- Hyperviscosity symptoms
- PP $>40\text{g/L}$ (IgG/IgA) or $>30\text{g/L}$ (IgM)

- We have a limited number of 2WW slots
- Please use appropriately!
- Advice and guidance requests answered daily
- Please use if unsure

Example referrals

- sFLC box ticked – no comment – ratio normal!
- X ray of ankle lytic lesion – no bloods done

2WW referral forms

SYMPTOMS AND CLINICAL EXAMINATIONS					
Leukaemia	<input type="checkbox"/>	Lymphoma (HD or NHL)	<input type="checkbox"/>	Myeloma	<input type="checkbox"/>
Teen and Young Adult (16–24 years) *SEND FORM SO PT TRACKED*					
<i>Note: There is a separate Children's referral form for pts <16 years.</i>					
Hepatosplenomegaly	<input type="checkbox"/>				– IMMEDIATE ASSESSMENT
Petechiae [2015]	<input type="checkbox"/>				– IMMEDIATE ASSESSMENT
Lymphadenopathy	<input type="checkbox"/>				– Call consultant
Splenomegaly	<input type="checkbox"/>				– Call consultant
Adults (>25 years)					
Lymphadenopathy	<input type="checkbox"/>				– FBC & CXR
<i>STOP: FBC suggests no lymphocytosis, follow local lymph node pathway</i>					
Splenomegaly	<input type="checkbox"/>				– FBC & CXR
If results of any of the following tests suggest myeloma:					-2WW
Serum Free Light Chain (SFLC)	<input checked="" type="checkbox"/>	FBC	<input type="checkbox"/>	U+E	<input type="checkbox"/>
Protein electrophoresis*	<input checked="" type="checkbox"/>	LFT	<input type="checkbox"/>	Bone profile	<input type="checkbox"/>
*If paraprotein <15mg with no symptoms/abnormalities, discuss with consultant					
Other primary cancer (specify):					

2WW referral forms

SYMPTOMS AND CLINICAL EXAMINATIONS					
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*if paraprotein <15mg with no symptoms/abnormalities, discuss with consultant					
Other primary cancer (specify):					

2WW referral forms

WHO PATIENT PERFORMANCE STATUS KEY	
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out light / sedentary work, e.g. house or school work.
2	Ambulatory and capable of self-care, but unable to carry out work activities. Up and active >50% of waking hours.
3	Capable of only limited self-care. Confined to bed or chair >50% of waking hours.
4	Completely disabled. Cannot carry out any self-care. Totally confined to bed or chair.

INVESTIGATIONS REQUIRED TO SUPPORT REFERRAL	
ALL HAEM CANCERS:	
FBC	<input type="checkbox"/>
19-Mar-2021 Full blood count	
19-Mar-2021 Equal 14.8 % Red blood cell distribution width	
19-Mar-2021 Equal 6.5 $10^9/L$ Neutrophil count	
19-Mar-2021 Equal 0.5 $10^9/L$ Lymphocyte count	Below low reference limit
19-Mar-2021 Equal 120.0 g/L Haemoglobin concentration	
19-Mar-2021 Equal 78.0 fL Mean cell volume	Below low reference limit
19-Mar-2021 Equal 26.2 pg Mean cell haemoglobin level	Below low reference limit
19-Mar-2021 Equal 0.1 $10^9/L$ Eosinophil count	- observation
19-Mar-2021 Equal 0.0 $10^9/L$ Basophil count	
19-Mar-2021 Equal 0.0 $10^9/L$ Nucleated red blood cell count	
19-Mar-2021 Equal 1.1 $10^9/L$ Monocyte count	- observation Above high reference limit
19-Mar-2021 Equal 0.36 Haematocrit	
19-Mar-2021 Equal 8.3 $10^9/L$ Total white blood count	
19-Mar-2021 Equal 4.58 $10^{12}/L$ Red blood cell count	
19-Mar-2021 Equal 377.0 $10^9/L$ Platelet count	- observation
Renal function/U+E	<input type="checkbox"/>

2WW referral forms

ADDITIONAL INFORMATION

Patient presented with continuous back pain, unintentional weight loss 8 kg in 8 months.

DISCUSSIONS WITH PATIENT PRIOR TO REFERRAL

Cancer needs to be excluded



Patient given referral information leaflet



Date(s) unavailable next 14 days:

Please attach a Patient Summary including:

Referral letter (if applicable)

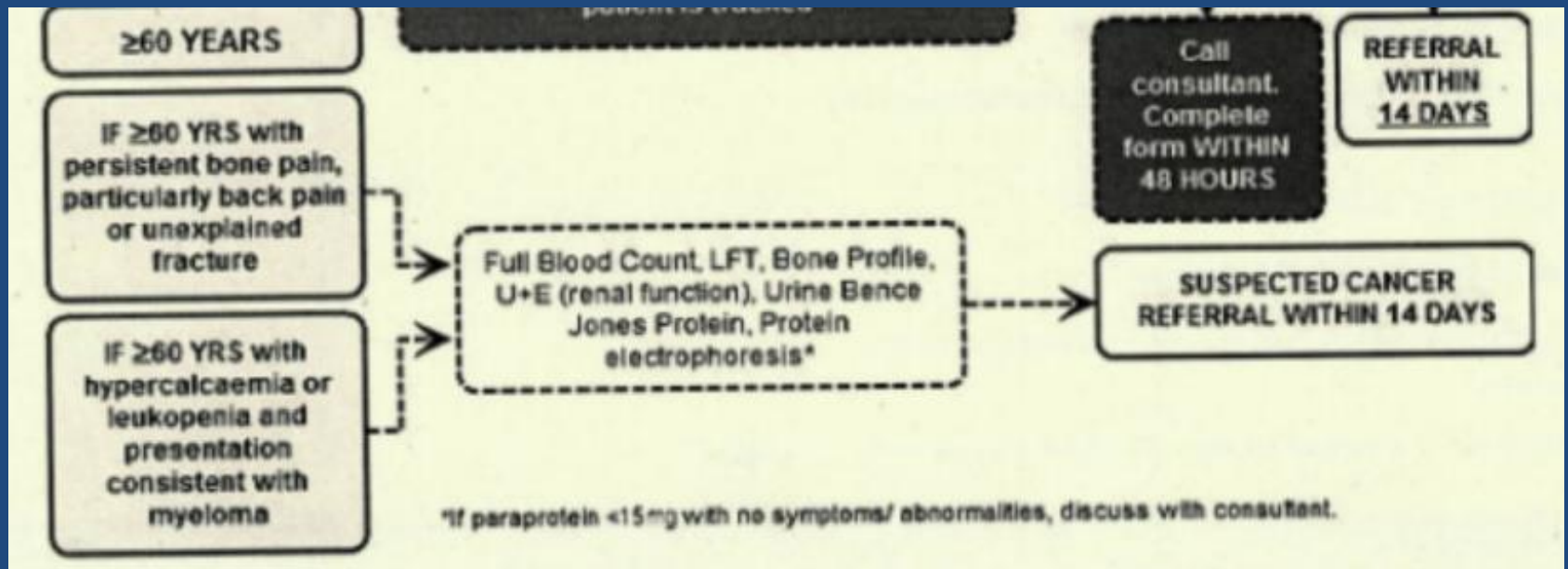
Investigation results

PMH

Up-to-date medications list and indications

If your patient does not meet NICE suspected cancer referral criteria, but you feel they warrant further investigation, please disclose full details in your referral letter.

2WW referral forms

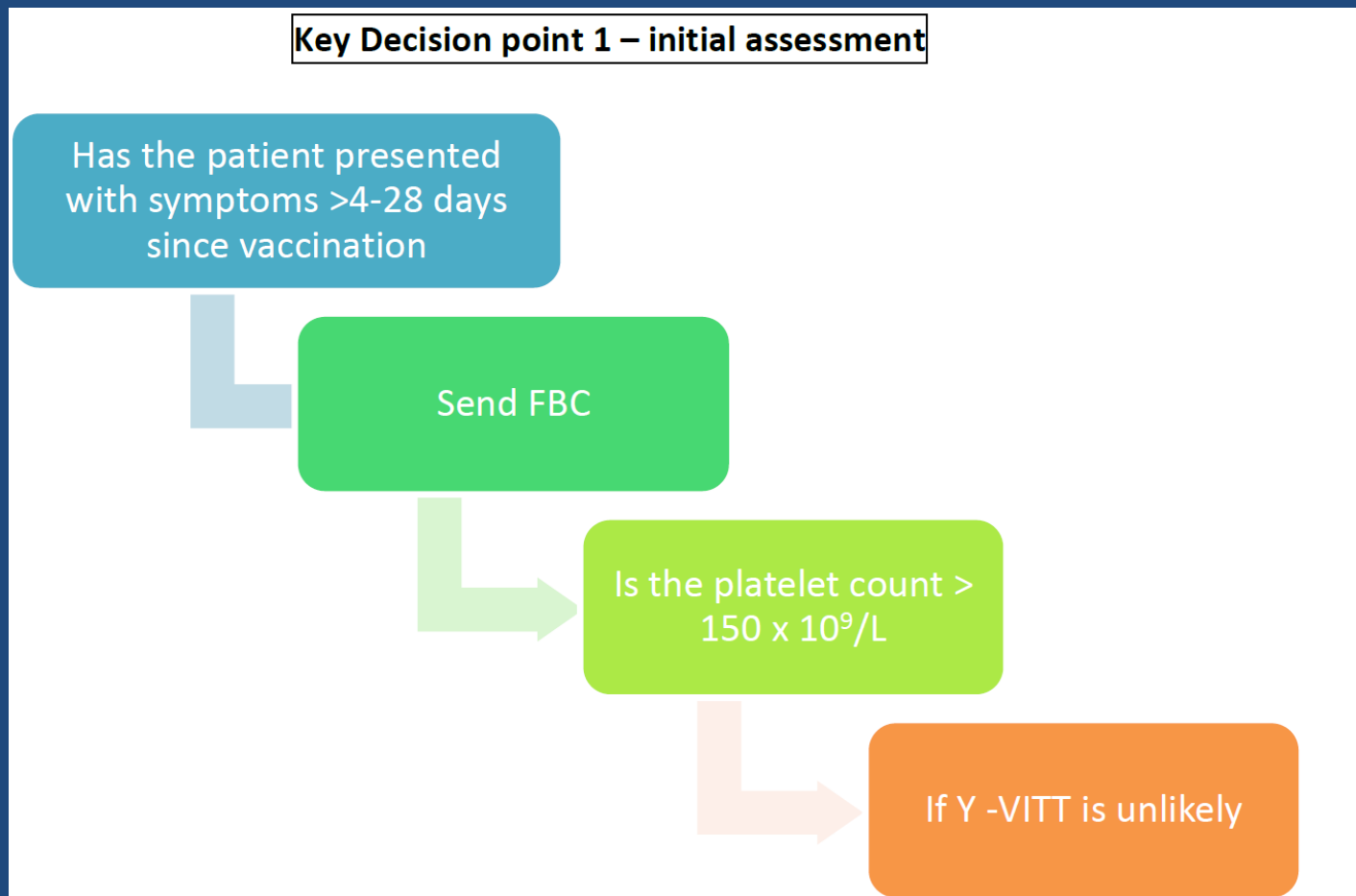


Vaccine induced thrombosis with thrombocytopenia (VITT)

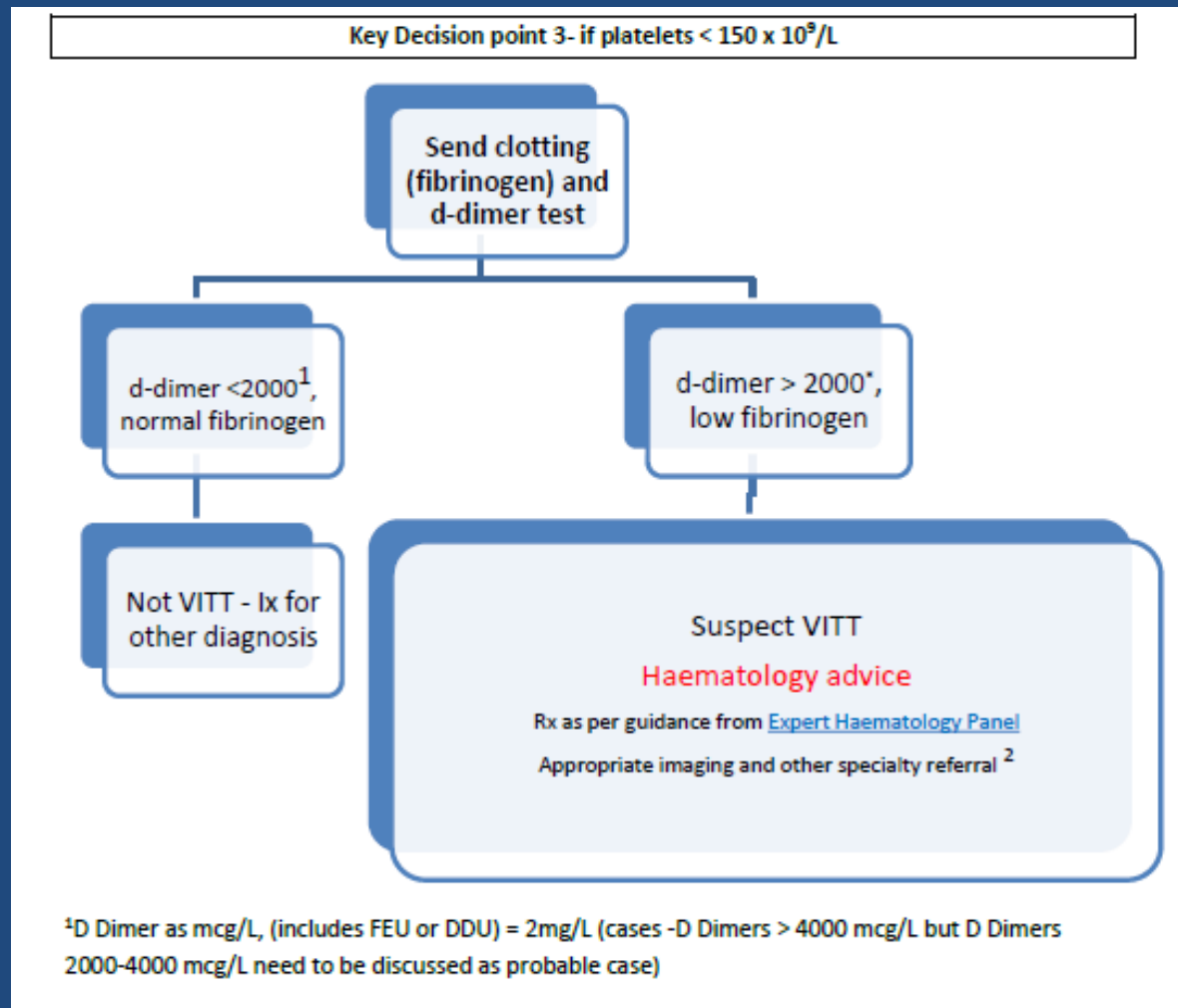
- BCSH website
 - Immune driven thrombosis, often cerebral venous sinus, portal or splanchnic venous thrombosis, and thrombocytopenia
 - After AZ Covid-19 vaccine
 - All ages and both genders

Vaccine induced thrombosis with thrombocytopenia (VITT)

- RC-EM guidance



Vaccine induced thrombosis with thrombocytopenia (VITT)



Vaccine induced thrombosis with thrombocytopenia (VITT)

- Can it be managed in primary care?
- RCGP guidance
 - Suspect if
 - New onset headache – not responsive to painkillers
 - Unusual headache
 - Worse on lying/bending
 - Blurred vision
 - N+V
 - Difficulty with speech
 - Weakness
 - Drowsiness
 - Seizures
 - New pinprick bruising or bleeding
 - SOB/chest pain/leg swelling/persistent abdo pain

Vaccine induced thrombosis with thrombocytopenia (VITT)

- Can it be managed in primary care?
- RCGP guidance
 - Reasonable to assess if patient
 - Not acutely unwell
 - FBC, D dimer and fibrinogen results will be reviewed and acted upon same day

Vaccine induced thrombosis with thrombocytopenia (VITT)

- BCSH
- Possible case
 - Acute thrombosis
 - New onset thrombocytopenia
 - Within 30 days of COVID vaccine
 - Investigations
 - FBC – plt <150
 - Coagulation screen + Fibrinogen + D dimers
 - Blood film

Vaccine induced thrombosis with thrombocytopenia (VITT)

- Unlikely case
 - Reduced platelets without thrombosis
 - D dimer at or near normal
 - Normal fibrinogen
 - Thrombosis with normal platelets
 - D dimer <2000
 - Normal fibrinogen

Vaccine induced thrombosis with thrombocytopenia (VITT)

- Probable case
 - D dimers >4000 (or >2000 + strong clinical suspicion)
 - Send serum PF4 ab assay
 - Look for CVST
 - US for portal or splanchnic thrombosis

Vaccine induced thrombosis with thrombocytopenia (VITT)

- Definite case
 - As above
 - PF4 abs +ve by ELISA

Summary

- Please utilize the 'Advice and Guidance' service
- Telephone Haem Secs only if urgent
 - no audit trail to these conversations
- Requests for 'special tests' incredibly useful prior to us seeing the patients
- We will recommend via the A+G response
- ICE request (live now)
 - JAK 2
 - BCR-ABL
 - Flow cytometry (immunophenotyping)
- Requires linked Haematology Consultant

- Thank you
- Any questions?
- Andrew.hodson@esneft.nhs.uk