Haematology GP Guidelines (TRFT)

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Rotherham Foundation NHS Trust, Version 6
Released November 2025, for review November 2029

ANAEMIA

Mild anaemia is often seen in those with chronic disease, and especially in males over 80years due to a variety of factors, this often does not warrant intervention if stable.

Please do not refer iron deficiency anaemia without prior discussion with a haematologist.

Additional tests	Considerations/ Management
Haematinics (B12, folate, ferritin)	Replace as necessary
Iron profile	Low transferrin saturation with ferritin <150 may support anaemia of chronic disease
LFT, U&E, TFTs,	Raised bilirubin may indicate haemolysis, consider renal anaemia if CrCl <40mls/min
Coeliac screen (TTG)	
Reticulocyte count	If elevated suggests bleeding, recent haematinic replacement or haemolysis
Serum immunoglobulins	?myeloma/ lymphoma
Haemoglobin electrophoresis	If persistent anaemia and variant haemoglobin suspected

CONSIDER URGENT DISCUSSION with on-call haematologist: new severe pancytopenia, suspicion of acute leukaemia, acute haemolytic anaemia

POLYCYTHAEMIA

DEFINITION

Persistently raised Hct:

• > 0.52 males • > 0.48 females

Suggest refer to exclude primary polycythaemia unless clear secondary causes

CONSIDER URGENT REFERRAL:

• Polycythaemia with Hct > 0.6 in males or > 0.56 in females in the absence of chronic hypoxia

• Hct > 0.52 in males or > 0.48 in females without clear secondary causes and in association with:

- Recent arterial or venous thrombosis
- Neurological symptoms

Possible causes:	Management
Respiratory: smoking, COPD, asthma, lung fibrosis, sleep apnoea	Check STOP-BANG score/Epworth Score for suspected OSA Consider oxygen therapy if sats < 93%
Cardiac (cyanotic heart disease)	As per parent team/cardiology
Drugs (anabolic steroids, testosterone, thiazide diuretics, SGLT2 inhibitors like empagliflozin)	For patients with hypogonadism, refer to guidelines e.g. European Andrology Academy. Consider switching thiazides to non-duiretic antihypertensives. SGLT2 drugs e.g. Empagliflozin, commonly elevate Hb, and should not be stopped for this reason.
EPO-secreting tumours (renal / liver tumours)	Control of malignancy +/- venesection
Relative – (plasma depletion) Dehydration, Poorly control diabetes mellitus, Excess alcohol	Control of underlying cause

MACROCYTOSIS

DEFINITION

Mean corpuscular volume (MCV) > 100 fl

If not associated with low Hb, low neutrophils, or low platelets, isolated macrocytosis is of doubtful significance.

Possible causes	Management
B12 / folate deficiency	Replace and monitor
Excess alcohol	
Liver disease including NAFLD	In cirrhotic patients with pancytopenia, consider discussion with hepatology.
Cytotoxic drugs (e.g. hydroxycarbamide, methotrexate)	No action may be needed if stable/longstanding
High red-cell turn-over e.g. haemolysis	Raised reticulocyte count and bilirubin –discuss with haem if cause unknown
Hypothyroidism	Check TSH
Myelodysplastic syndromes	Refer if concerned about progressive cytopenias
Myeloma	Check immunoglobulins

NEUTROPENIA

DEFINITION

Neutrophil count under normal laboratory range. Infection risk is most significant when <0.5 1 x 10^9 /L

- Mild: 1 – 1.5 x 10^9 /L
- Moderate: 0.5 – 1 x 10^9 /L
- Severe: < 0.5 x 10^9 /L

Possible Causes	Considerations
Benign Ethnic Neutropenia –(Now termed 'Duffy Null Associated Neutropenia'	Normal range can be lower for non-white ethnicities commonly 1.0-1.5 x 10^9/L Refer for Duffy blood group testing only if this will change management.
Viral infection	May cause a transient neutropenia. Consider testing for EBV, CMV, HIV HepB and HepC depending on presentation.
Sepsis	Especially in elderly or alcohol excess
Autoimmune disease	Often variable, and longstanding
Bone marrow failure (aplasia, myelodysplasia, malignant infiltration)	By exclusion of alternative causes, usually as part of pancytopenia
B12 / folate deficiency	Replace and monitor
Thyroid disease	Screen and treat as necessary
Drugs: High dose antibiotics e.g. penicillin, trimethoprim, Cytotoxic agents, Antithyroid medication, Anti-epileptics e.g. valproate, clozapine	Consider interruption dependent on scenario/ alternatives. Liaison with parent speciality.

LYMPHADENOPATHY

Lymph nodes (up to 1.5 cm in the groin, and 1cm at other sites) are palpable in many normal persons and may be considered normal structures if stable and low volume.

If a malignant cause is suspected: refer female patients with axillary nodes via the breast pathway, and isolated neck nodes via ENT.

Incidental splenomegaly on imaging <13cm should not be referred unless there are clinical features of concern. Consider liver disease and interval imaging as appropriate.

1- Check FBC + film, biochemical profile, calcium and LDH. Consider HIV testing.

2- Consider glandular fever in patients < 25yrs: EBV IgM and IgG testing may be useful.

The following should be referred urgently for outpatient assessment:

a. Unexplained lymphadenopathy of over 2 cm (persistent for > 6 weeks) and/ or

b. palpable splenomegaly

c. Lymphadenopathy for <6 weeks in association with:

- B symptoms – fevers/sweats/weight loss
- Hepatic or splenic enlargement
- Rapid nodal enlargement
- Disseminated/generalised nodal enlargement
- Anaemia/leucopenia/thrombocytopenia
- Hypercalcaemia

3-

LYMPHOCYTOSIS

Most raised lymphocyte counts in general practice are reactive. Acute and transient episodes are commonly seen post viral infection.

Chronic and low grade lymphocytosis (4.0 - 7.0 x 10^9 /l) may be seen in metabolic syndromes and asplenic states, these are usually non progressive and do not require haematological referral.

Monitoring, if undertaken, can be every 12 months unless there is clinical concern in which case clinical opinion can be requested.

The following should be referred urgently for outpatient assessment:

- Suspicion of lymphoma / leukaemia with a lymphocytosis in association with:
  - Anaemia, thrombocytopenia or neutropenia
  - Splenomegaly
  - Lymphadenopathy
  - B symptoms (weight loss, night sweats, fever)

Consider routine referral if persisting lymphocytosis >10 x 10^9 /L not fulfilling criteria for urgent referral.

LEUCOCYTOSIS

DEFINITION

■ WCC > 10 x 10^9 /l

Leucocytosis caused by a haematological malignancy is usually indicated from examination of a blood film, look for medical comments about causation on your results system.

	Findings	Management
	Unexplained WCC >50	Discuss with on call Haematologist
	Blood film suggestive of Chronic Myeloid Leukaemia or Acute Leukaemia	As per blood film comments –discuss with on-call haematologist via phone as indicated.
	Persistent monocytosis with cytopenia	Refer to Haematology, unless there is an ongoing infective cause.
	Persistent low level neutrophilia (<15) +/- mild lymphocytosis and monocytosis.	Often seen in chronic inflammation/ smokers/ metabolic syndrome. Should not be referred without other features of concern
	Blood film features indicating either dysplasia or primary myeloproliferative disease	Refer unless cause known
	New elevated WCC without clear cause	Perform relevant investigation to exclude occult infection and malignancy. Haem A+G if unclear

EOSINOPHILIA

Usually secondary (see table below). Eosinophilia can rarely cause end organ damage, e.g. cardiac, gastro, pulmonary, neurological systems: consider this (+urgent haematology referral) if new/evolving symptoms in presence of Eosinophils >1.5, assuming no established secondary causes.

	Eosinophil count	Management
	Mild: 0.46 - 1.5 x 10^9 /l	Consider interval testing and differentials as below
	Moderate: 1.5 - 5.0 x 10^9 /l	If end organ damage: urgent referral
	Severe: > 5.0 x 10^9 /l	Urgent referral unless known cause

Possible Causes	Management
Allergy / atopy	E.g. Asthma/Eczema. Testing IgE levels may be useful
Infection (especially parasitic)	May require input from ID if travel history
Inflammation (connective tissue disease / vasculitis)	If known, consider discussing with relevant speciality.
Solid tumour (lung, renal, breast)	Usually apparent from history
Lymphoma (Hodgkin, T-cell non-Hodgkin)	Usually apparent from history
Drugs e.g. Penicillin, anti-epileptics, Sulphur drugs	

THROMBOCYTOSIS (High Platelet Count)

DEFINITION

· Platelet count > 450 x 10^9/L

· Very high platelet counts in myeloproliferative disorders increase the risk of thrombosis and abnormal bleeding due to platelet dysfunction.

Possible Causes	Management
· Reactive causes (e.g. acute/chronic inflammation, infection, recent surgery, malignancy, bleeding)	May take up to 6w to settle after major inflammatory insult, check CRP, and exclude malignancy depending on history.
· Iron deficiency	Correlate with ferritin, T sats
· Essential thrombocythaemia	Associated with increased thrombosis risk, pseudohyperkalaemia

	Platelet count	Management
	· Platelet count > 1000 x 10^9/L	Urgent referral (unless cause known (e.g. within 6w of major abdominal surgery)
	· Platelet count 450 – 1000 x 10^9/L with: recent arterial or venous thrombosis, or abnormal bleeding	Urgent referral suggested
	Platelet count 450 – 1000 x 10^9/L nil of above	Investigate and treat iron deficiency, investigate and manage reactive causes: malignancy, infection, bleeding. Repeat in 6w, and consider referral if no reactive causes and platelets remain high
	Borderline cases	Discuss via eRS, Haematology A+G

THROMBOCYTOPENIA (Low Platelet Count)

DEFINITION

· Platelet count < 150 x 10^9/L

· Most patients with platelet count > 50 x 10^9/L are asymptomatic

· Risk of spontaneous bleeding significantly increases if platelet count < 20 x 10^9/L

	Platelet count/ clinical features	Considerations	Management
	Platelets <20 x 10^9/L or active bleeding with platelets <30	Rule out known causes or diagnosis e.g. ITP	Discuss with on-call haematologist
	Platelets 20-50 x 10^9/L (ensure repeated)	If known liver disease, discuss with Hepatology if concerned Exclude drug causes, alcohol, liver disease, b12/folate deficiency, check clotting, Hepatitis and HIV testing, UE and LFTs	Urgent referral to haematology if cause unclear.
	Low platelets 50-100 x 10^9/L + other features of concern e.g. Hb <100, neutrophil count <1.0	Exclude drug causes, alcohol, liver disease, b12/folate deficiency, check clotting, Hepatitis and HIV testing, UE and LFTs	Urgent haematology referral for pancytopenia without cause.
	Isolated low platelets 50-150 x 10^9/L, no known cause	Exclude drug causes, alcohol, liver disease, b12/folate deficiency, check clotting, Hepatitis and HIV testing, UE and LFTs	Isolated low platelets are rarely indicative of bone marrow failure. Routine referral to haematology if cause unclear.

PARAPROTEIN/ MONOCLONAL IMMUNOGLOBULINS

The finding of a monoclonal immunoglobulin may represent asymptomatic MGUS (Monoclonal Gammopathy of Uncertain Significance), myeloma or a lymphoma. A locally applied score 1 (low), 2 (intermediate) and 3 (high) attempts to predict the chance of clinically significant disease based on laboratory parameters alone. MGUS is asymptomatic and increasingly found in older age: 1% of 50 yr olds, and 10% of 85 year olds.

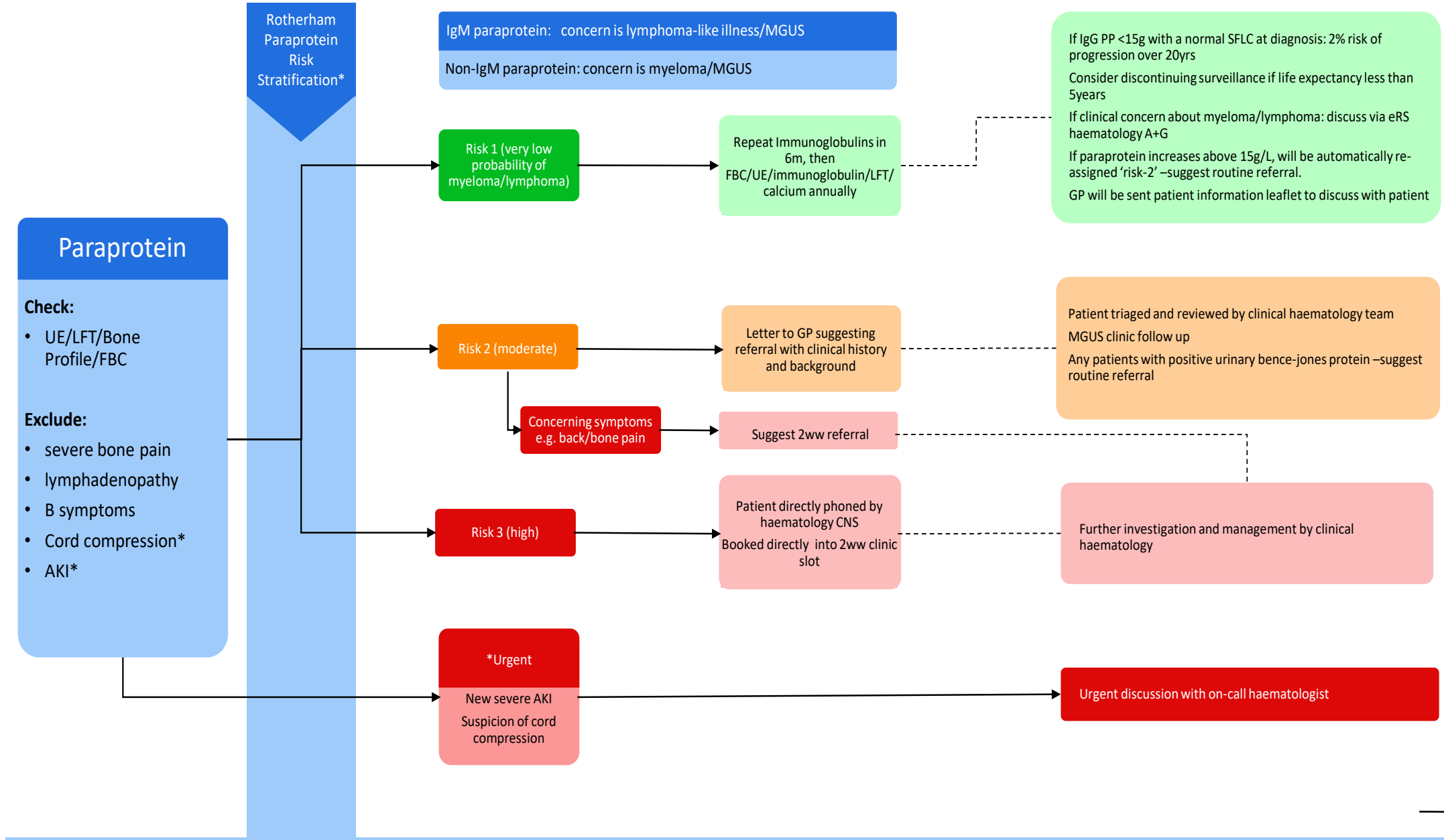
Elevated immunoglobulins without a monoclone is non-specific and are not indicative of haematological disease. Please refer to the following chart for guidance on management of a new monoclonal protein.

For new MGUS patients: We are grateful for GPs monitoring low risk (risk 1) patients, as per chart below, suggest providing patient information such as: https://www.myeloma.org.uk/library/monoclonal-gammopathy-of-undetermined-significance-mgus-infosheet/

When a new monoclone is found, the laboratory will automatically add a serum free light chain assay to help with risk stratification. This is not routinely required for the monitoring of low-risk MGUS. The ratio of kappa:lambda chains is key with a ratio of 0.37-3.1 being normal in many patients, and a ratio of <0.01/ >100 indicative of myeloma.

Monoclonal gammopathy of unk

LINK TO LOCAL PATIENT INFORMATION LEAFLET



*Rotherham Paraprotein Risk Stratification: based on type and height of paraprotein, Serum Free Light Chain assay (automatically added to a new paraprotien), Hb, Cr, immunoparesis. Estimates probability of clinically significant disease as an adjunct to clinical judgement. Please discuss via eRS 'Advice and Guidance' if there is clinical concern about an inappropriate risk-score.

Abnormal Bleeding/Bruising or Abnormal Coagulation Tests

The best assessment for identifying a bleeding disorder is in the history. Document the anatomical sites of bleeding symptoms, time-course and severity. The likelihood of a bleeding disorder is greater if bleeding occurs at multiple sites and is severe (e.g. prolonged nose bleeds >30 minutes or requiring treatment from an ENT specialist, heavy periods requiring medical or surgical treatment, traumatic bleeding requiring hospital treatment). Bleeding after more than one surgical or dental procedure or persistent bleeding over months or years is suggestive of bleeding disorder. By contrast, features such as easy bruising, other bleeding symptoms at a single anatomical site and only one episode of abnormal bleeding do not suggest a bleeding disorder.

Consider the following:

- Vascular disorders such as senile or solar purpura: commonly affecting the extensor surfaces hands and arms in older individuals, this is not suggestive of a bleeding disorder unless associated with more widespread bleeding and bruising.
- Drugs including steroids, alcohol, anti-platelets, anticoagulants, other drugs such as SSRI's can cause easy bruising and minor bleeding.
- Family history: An inherited bleeding disorder is more likely if similar bleeding symptoms occur in other close family members
- Previous haemostatic challenges: Absent bleeding after multiple surgical or dental procedures suggests that there is not a bleeding disorder.
- A 'clotting' or coagulation screen is a poor predictor of clinically significant bleeding disorders, and does not perform well in a community setting.

Acute unexplained abnormal bleeding/bruising: Check and urgent FBC, UE, LFT (+coagulation screen if can be delivered to the lab within 4 hours of venepuncture). If severe, discuss with on call haematologist.

Longstanding unexplained abnormal bleeding/ bruising: assuming FBC, UE and LFT completed, consider onward referral to haematology if the history is suggestive. Community coagulation screen blood testing not routinely recommended.

If a coagulation screen has been performed and shows isolated raised APTT (not on anticoagulants):

- This is often artefactual. Samples are only stable for 4 hours in the blood sample tubes, the APTT will progressively rise in older samples.
- Incidental finding with no bleeding history and no surgery planned: Consider repeat clotting requesting an 'ACTIN-FS APTT' / consider phlebotomy in hospital to minimise transit time. If normal -no further action required.
- Consider onward referral of those with an unexplained long APTT and a bleeding history, or those who have not had any haemostatic challenges (young patients with no prior surgery/ dental extractions)