NHS LANARKSHIRE

Common Haematology Referrals

Dr Jane Clark, Consultant Haematologist. Review Date 01/04/2025

NHS LANARKSHIRE
Common Haematology Referrals
April 2022

This document is designed to help guide further investigations and referral in patients with abnormal haematology blood results.

There is a duty haematologist available for urgent advice on all 3 sites during office hours and calls should be directed to the catchment hospital.

A consultant haematologist is available out-of-hours at all times for urgent advice and can be contacted through any NHSL hospital switchboard.

In-patient haematology care in Lanarkshire is centralised in Monklands Hospital (ward 16) and is covered on a rotational basis by all 9 consultants. There are out-patient clinics and day wards on all 3 NHSL sites. Systemic anti-cancer therapy is only delivered at University Hospitals Monklands and Hairmyres. Direct admission to the in-patient haematology ward (ward 16 UHM) is not currently possible due to Covid restrictions.

CONTENTS

1. PARAPROTEIN BAND

The presence of a paraprotein band raises the possibility of an underlying plasma cell disorder. IgM paraproteins are **rarely** found in myeloma and may indicate a lymphoproliferative disorder.

Tests in primary care

- FBC, ESR, Renal function, LDH, LFTs and Ca
- Urinary Bence-Jones proteins
- Serum free light chains (separate golf top sample)
- Immunoglobulins and serum electrophoresis

Urgent referral to haematology is indicated if a paraprotein band is found **AND** associated with other features of myeloma, lymphoproliferative disorder (usually IgM) or amyloidosis.

Myeloma	**Lymphoproliferative Disorder**	**Amyloidosis**
Hypercalcaemia	Lymphadenopathy	Macroglossia
Bone pain/lytic lesions	Hepatosplenomegaly	Nephrotic Syndrome
Unexplained anaemia	B Symptoms	Neuropathy
Unexplained renal failure	Symptoms of hyperviscosity	Unexplained heart failure
IgG band >15g/l IgA >10g/l BJP >500mg/l (24h collection) Abnormal SFLC ratio	Pancytopenia IgM band >10g/L	Carpal tunnel syndrome

Routine referral for all others with a paraprotein band not meeting above criteria**.**

Monoclonal Gammopathy of Undetermined Significance (MGUS) is the presence of a monoclonal protein in the serum or urine with no other features of myeloma. MGUS is present in 1% of the population. The incidence increases with age with about 5% of over 70s having a detectable paraprotein band. There will be no clinical implications for the majority of these patients.

Patients have a very low risk of progression to myeloma if:

- Ig G <15g/l
- Ig M / A <10g/l
- Normal SFLC
- No significant BJ proteinuria
- AND no symptoms

Although it is common practice in NHSL to monitor these patients at nurse-led clinics, anyone not fit enough to attend hospital can be monitored in primary care. FBC, U&Es, Ca and paraprotein band should be monitored 3-4 monthly for the first year and then, if stable, every 6 to 12 months. Patient information sheet is available at www.macmillan.org.uk

Patients being monitored should be referred to haematology if they develop:

- Symptoms as listed above
- Unexplained anaemia (not due to haematinic deficiency) / other cytopenias
- Unexplained renal impairment
- Rise in paraprotein band >25% (at least 5g/l)
- Hypercalcaemia

Please note:

- Patients with isolated or polyclonal raised immunoglobulins in the absence of a paraprotein band in the serum electrophoresis **do not require referral** to haematology. Hypergammaglobulinaemia implies non-specific immune reaction and is not associated with underlying haematological disorders. Consider liver disease, immune response and connective tissue disorders.

2. LEUCOCYTOSIS

Elevation of white cell count above laboratory reference range (>11 x 10^9/l)

Wide differential, ranging from a normal response to acute infection/active inflammation or acute stress (e.g. acute bleed, ACS), through to haematological malignancies including acute leukaemias. A high white cell count can also be seen in solid malignancies, steroid use and smoking.

Suggested tests in primary care

- Careful history and assessment for reactive cases as stated above
- Differential white cell count (see separate referral criteria for lymphocytosis, eosinophilia, monocytosis) and other FBC parameters
- Blood film (please request in additional test box)
- Assess for presence of lymphadenopathy or splenomegaly
- Biochemistry including renal and liver function, LDH calcium, urate, albumin
- ESR and CRP
- Urinalysis
- CXR

Criteria for **urgent** admission (telephone for admission – in most cases we will have contacted GP due to abnormal indices and blood film appearances)

- New suspected acute leukaemia
- New suspected chronic myeloid leukaemia with either white cell count >100 x 10^9/l or symptoms of hyperviscosity (headaches / visual disturbance / thrombosis)

Criteria for **urgent** referral (out-patient assessment)

- Leucoerythroblastic blood picture (from blood film report – presence of immature white cells and nucleated red blood cells)
- New CML not meeting above criteria
- Unexplained increased white cell count >50 x 10^9/l

Criteria for **routine** referral (out-patient assessment)

- Significant leucocytosis >20 x 10^9/l after 6 weeks and no obvious reactive cause

Who does not require referral?

- Transient neutrophilia or persistent, mild neutrophilia < 15 x 10^9/l. Most likely associated with a chronic inflammatory / infective process or smoking (**a neutrophil count of up to 12.5 x 10^9/l can be considered normal in smokers**).

3. NEUTROPENIA

Isolated neutrophil count below laboratory reference range (<2.0 x10^9/l)

Neutrophil count	Severity	Infection risk
1.0 – 1.8 x 10^9/l	Mild	No significant risk of infection
0.5 – 1.0 x 10^9/l	Moderate	Some increase in risk
< 0.5 x 10^9/l	Severe	Major increase in risk

Review ethnicity of all patients. A neutrophil count between 1.0-2.0 x 10^9/l is normal in people of West African, Afro-Caribbean and Middle Eastern ancestry.

Patients with mild neutropenia are not generally at increased risk of infection.

Viral infection / sepsis commonly cause neutropenia which is transient.

Common drugs that can cause neutropenia include antipsychotics / sulphonylureas / propylthiouracil / carbimazole / sulphonamides / cotrimoxazole / bendroflumethazide / anticonvulsants / NSAIDs / and ranitidine. This list is not exhaustive – please consult BNF.

Suggested tests in primary care

- Assess ethnicity (see above)
- Assess patient for symptoms (recurrent infections / mouth ulcers / thrush)
- Examine for lymphadenopathy and splenomegaly
- Repeat FBC
    - If neutrophils > 1.0 x 10^9/l, repeat at 6 weeks
    - If neutrophils < 1.0 x 10^9/l, repeat at 1 week
- If neutropenia persists on repeat testing request
    - Blood film
    - B12 / folate
    - ANA
    - HIV serology
    - U+E, LFTs, Ca, GGT, CRP, LDH

Criteria for **urgent** hospital admission

- Neutrophil count of <1.0 and post-chemotherapy with evidence of sepsis
- Neutrophil count of <0.5 consider admission if new finding or clinical concern

Criteria for **urgent** referral (out-patient assessment)

- Neutropenia associated with other cytopenias (Hb <100g/l, PLT <50 x 10^9/l, unless this is due to established liver disease)
- Neutropenia associated with lymphadenopathy and/or splenomegaly

Criteria for **routine** referral (out-patient assessment)

- Neutrophils <1.0 on repeat testing
- Neutrophils <2.0 on repeat testing and the presence of any of the clinical findings described above
- Consider calling for advice in first instance if there is uncertainty about whether a referral is indicated

Who does not require referral?

- Neutrophils consistently >1.5 but <2.0. These patients can be given the diagnosis of chronic idiopathic neutropenia. No further monitoring required.
- Neutrophils >1.0 but <1.5, recheck annually. Refer if neutrophils fall <1.0 or clinical picture of concern. Otherwise label as chronic idiopathic neutropenia.
- Anticipated neutropenia due to medication (e.g. methotrexate / anticonvulsants). The decision on whether this should be discontinued should be discussed with the relevant specialty.

4. THROMBOCYTOSIS

Persistent increase in the platelet count above 450 x 10^9/l

Reactive causes (secondary) are much more common than primary bone marrow disorders (myeloproliferative conditions). Causes of a reactive thrombocytosis include infection / inflammation / bleeding or iron deficiency / recent surgery or trauma / hyposplenism / drugs (steroids) / malignancy / connective tissue disorders.

A primary cause is more suggestive if there is an accompanying erythrocytosis or leucocytosis, arterial or venous thrombotic events or abnormal bleeding (due to platelet dysfunction).

Suggested tests in primary care

- History and examination (clues to reactive cause)
- Serial FBCs (>3m apart)
- Blood film (please request in additional test box)
- ESR and CRP
- Ferritin +/- iron studies
- Renal and liver function

Criteria for **urgent** referral (out-patient assessment)

- Persistent thrombocytosis >600 (>3m apart), with no apparent reactive cause
- Persistent thrombocytosis >450 (on at least 2 occasions 4 weeks apart), in patients with an acute clot (arterial or venous)

Criteria for **routine** referral (out-patient assessment)

- Persistent thrombocytosis >450 for at least 3 months with no apparent reactive cause

When referring patients with a persistent thrombocytosis, please send 1 x EDTA (purple) tube for "JAK2 mutation analysis" to haematology at time of referral.

Who does not require referral?

- Persistent thrombocytosis with a known reactive cause (no increased risk of thrombosis)

5. THROMBOCYTOPENIA

Platelet count below laboratory reference range (<140 x 10^9/l)

The majority of patients with a platelet count of >50 x 10^9/l are asymptomatic and have a low bleeding risk. The risk of spontaneous bleeding increases significantly below 20 x 10^9/l.

Platelet type bleeding is usually bruising / petechiae / bleeding from mucous membranes (epistaxis, GI or GU bleeding). The actual risk of intra-cranial haemorrhage is low.

Causes

- Drug induced (review all medications and consider stopping drug(s) that may be implicated. Commonest are heparin, quinine, bendroflumethazide, sulphonamides, sulphonylureas, phenytoin, methotrexate, ranitidine, NSAIDS (this list is not exhaustive)
- Alcohol (thrombocytopenia can resolve after a period of abstinence)
- Hypersplenism and non-alcoholic steatohepatitis
- Immune (ITP)
- Infection and sepsis
- Any cause of BM failure
- DIC
- TTP / HUS

Suggested tests in primary care

- Assess patients for bleeding / bruising
- Review all medications
- Assess alcohol intake
- Examine for lymphadenopathy and splenomegaly
- Blood film (**exclude platelet clumping artefact**) (please request in additional test box)
- B12 and folate (treat if found to be deficient)
- ANA
- HIV, Hepatitis B and C serology
- LFTs, AST, GGT and renal function

Criteria for **urgent** referral for hospital admission

- Platelet count <50 and bleeding

Criteria for **urgent** referral (out-patient assessment)

- Isolated platelet count < 50, not bleeding, no known cause

- Platelet count 50-100
    - With an accompanying cytopenia(s), (Hb<10.0, neutrophils <1.0)*
    - With splenomegaly
    - With lymphadenopathy
    - In pregnancy
    - In a patient with planned surgery

Criteria for **routine** referral

- Persistent platelet count <100 (on at least 2 occasions 6 – 8 weeks apart) and no known cause

Who does not require referral?

- Isolated platelet count 100-150 with no accompanying clinical features
- Thrombocytopenia due to liver disease – this should be discussed with gastroenterology
- If platelets are >100, repeat at 6 months, if remains >100, no requirement for ongoing monitoring.
- Thrombocytopenia due to platelet clumping – this is of no clinical significance and if an accurate platelet count is required, please send a citrate sample (pale blue top) with the form clearly marked “for platelet count - previous platelet clumping”

6. LYMPHOCYTOSIS

Lymphocyte count above laboratory reference range (> 4.0 x 10^9/l)

A transient reactive lymphocytosis can be seen in acute viral infections (particularly infectious mononucleosis), acute chest pain, status epilepticus etc.

Smoking is a well recognised cause of a reactive lymphocytosis and is often associated with mild neutrophilia and monocytosis.

Suggested tests in primary care

- Blood film if lymphocytes > 5 x 10^9/l (will be done by reflex in laboratory)
- Repeat FBC in 8 weeks if lymphocyte count 6-10 x 10^9/l (viral lymphocytosis is frequently transient)
- Monospot test and inflammatory markers
- LFTs
- Viral serology for EBV / CMV / HIV / hepatitis B and C (if relevant symptoms)
- Immunophenotyping (Cell Markers) if lymphocytes are > 6 x 10^9/l for >2 months Please send 1 x EDTA (purple) sample to lab for cell markers. Sample should be sent at start of working week i.e. Mon-Wed.

Criteria for **urgent** referral (Out-patient assessment)

- Lymphocytosis in association with anaemia, thrombocytopenia or neutropenia
- Symptomatic patients (weight loss, fever, drenching night sweats), palpable lymphadenopathy >1cm and / or splenomegaly
- Immunophenotyping results suggest a clonal B cell lymphocytosis (that is **not** CLL).

Criteria for **routine** referral (Out-patient assessment)

- Immunophenotyping results suggest a clonal B cell population with CLL in an asymptomatic patient with no cytopenias, lymphadenopathy or B-symptoms.

Who does not need referral?

- Lymphocytosis < 6 x 10^9/l
- Asymptomatic patients with a one-off isolated lymphocytosis 6-10 x 10^9/l. Repeat FBC in 8-12 weeks.

7. LYMPHOPENIA

Lymphocyte count below the laboratory reference range (<1 x 10^9/l)

Its significance should be judged in light of age, clinical details and other results. It is a common non-specific finding.

Common causes include acute and chronic infections (including HIV), corticosteroids, cardiac failure, connective tissue disorders, uraemia, chemotherapy and carcinoma. Rarely is it due to lymphoma.

Any B symptoms (weight loss, night sweats or unexplained pyrexia) or lymphadenopathy ***may*** suggest lymphoma.

Suggested tests in primary care

- Blood film (please request in additional test box)
- Renal and hepatic function
- ANA
- HIV serology
- Immunoglobulins and serum electrophoresis

Criteria for referral (Out-patient assessment)

- B symptoms as above
- Lymphadenopathy > 1cm and /or splenomegaly

Who does not need referral?

- Isolated lymphopenia in an otherwise well patient with normal exam findings and negative investigations
    - Repeat at 6 months, if no change then no further monitoring is required

8. MONOCYTOSIS

Monocyte count above the laboratory reference range (>1.0 x 10^9/l)

Monocytosis is commonly caused by chronic inflammatory or infective problems such as TB / endocarditis / SLE / rheumatoid arthritis / temporal arteritis.
Patients on steroids and smokers can have a monocytosis, usually in association with neutrophilia. A mild chronic monocytosis can be expected in ex-smokers and does not require investigation.

The most common primary haematological cause of chronic monocytosis is myelodysplasia (WHO subtype chronic myelomonocytic leukaemia (CMML)). Usually the patient will have a macrocytosis and additional blood cytopenias in addition to a monocytosis. It may be suggested by a blood film, but a bone marrow test is required to confirm.

Pseudomonocytosis with artefactual storage change is common.

Suggested tests in primary care:

- When first identified
    - Monocyte count ≥ 2 x 10^9/l, repeat at 6-8 weeks
    - Monocyte count ≥1.0 but < 2 x 10^9/l, repeat at 3 months.
- If on repeat the monocytosis is resolved, no further investigations are required.
- If the monocytosis persists request blood film and CRP

Criteria for referral (Out-patient assessment)

- All patients with an unexplained persistent monocytosis **ie monocyte count > 2 x10^9/l** (> 3m apart)
- Monocytosis with any additional FBC abnormality i.e. anaemia (Hb <110), macrocytosis MCV > 105, neutropenia or thrombocytopenia.

Who does not need referral?

- Monocytosis with evidence of an inflammatory or infectious cause. It may be appropriate in this instance to refer to an alternative specialty.
- Monocytosis in a smoker

9. EOSINOPHILIA

An increase in eosinophils above laboratory reference range (>0.5 x 10^9/l)

Eosinophilia is usually reactive; associated with allergy / asthma / connective tissue disorders / drugs / parasitic infections (particularly in children)/ malignancy (not just haematological malignancy). Rarely, primary haematological malignancies can be associated with an eosinophilia.

A persistent increase in eosinophils > 2 x 10^9/l can be associated with organ toxicity.

Investigation is appropriate if eosinophils are raised >0.5 x 10^9/l for over 8 weeks and no obvious cause is apparent.
Earlier investigation is appropriate if eosinophils are > 2.0 x 10^9/l with no obvious reactive cause.

Suggested tests in primary care

- Assess travel history, allergic reactions, drugs
- FBC
- Blood film (please request in additional test box)
- Inflammatory markers (CRP)
- Biochemistry including renal and liver function, LDH, calcium, albumin and urate
- CxR
- Urinalysis (? Proteinuria)
- Consider vasculitis screen (ANCA, ANA etc)
- Stool x 3 for ova, cysts and parasites

Criteria for referral (Out-patient assessment)

- Persistent eosinophilia > 2 x 10^9/l for > 6m, with no obvious reactive cause.

Who does not need referral?

- Reactive eosinophilia may require assessment by other specialties i.e. rheumatology, respiratory, renal, infectious diseases depending on the cause.

10. POLYCYTHAEMIA

Elevated haemoglobin (Hb) concentration and raised Packed Cell Volume (PCV)/Haematocrit (Hct)

Spurious or **apparent:** due to reduced plasma volume associated with diuretics, dehydration, alcohol.
Secondary: most commonly due to hypoxia (smoking, chronic lung disease, congenital heart disease).
Primary: myeloproliferative neoplasm, polycythaemia vera. There may be accompanying leucocytosis or thrombocytosis.

The JAK 2 mutation is positive in 97% of patients with PV.

Suggested tests in primary care

- Serial FBCs at least 2 months apart
- Serum ferritin and iron studies
- Evaluate the patients for any possible secondary cause and where possible correct these factors
- CXR, SpO2
- Check JAK2 (EDTA sample), if Hct >0.52 in males or 0.48 in females on at least 2 occasions 8 weeks apart with no obvious reactive cause.
- Check JAK2 even on first occasion, if Hct >0.52 in men and >0.48 in women and there is an associated unexplained rise in white cells or platelets or associated arterial/venous clot, itch (classically aquagenic) or splenomegaly.

Criteria for **urgent** referral (Out-patient assessment)

- Hct > 0.60 in men or >0.56 in women in the absence of chronic hypoxia
- Hct >0.52 in men and >0.48 in women associated with an unexplained rise in white cells or platelets or associated with arterial/venous clot, itch (classically aquagenic), splenomegaly.

Criteria for **routine** referral (Out-patient assessment)

- Persistently raised unexplained Hct >0.52 in men and >0.48 in women for at least 8 weeks in an asymptomatic patient.

Who does not need referral?

- If the polycythaemia is associated with hypoxia / lung disease, initial referral to the cardiology or respiratory team may be more appropriate. Venesection is rarely indicated in these patients.

11. ISOLATED MACROCYTOSIS

MCV above laboratory reference range (>100fl) with all other FBC indices being normal. Please note that MCV values will increase between 5-10% if there is a delay in sample processing. Macrocytosis is a normal physiological finding in pregnancy.

Suggested tests in primary care

- Assess alcohol intake (check GGT)
- Blood film (please request in additional test box)
- Check B12 and folate if MCV >104 or there are cytopenias (replace if deficiency detected)
- Reticulocyte count
- LFTs (chronic liver disease)
- TFTs (hypothyroidism)
- Protein electrophoresis / immunoglobulins / urine for Bence-Jones protein
- Review medications. Seen routinely in patients on methotrexate / sulphasalazine / hydroxycarbamide / antiretrovirals

Criteria for referral (Out-patient assessment)

- Macrocytosis with dysplastic features on a blood film (suggested on a film comment)
- Macrocytosis with increased reticulocytes
- Macrocytosis with any additional FBC abnormality (unless due to B12/folate deficiency)

Who does not need referral?

- Macrocytosis due to alcohol excess / haematinic deficiency if corrects on replacement / liver disease / drug cause / hypothyroidism (should normalize on treatment)

Uncomplicated B12 or folate deficiency does not require referral to haematology.

12. NIGHT SWEATS

Drenching night sweats that soak bed clothes or bedding.

This is a common non-specific symptom and the majority of patients do not have a haematological malignancy.

Medical causes vary and include -

- Infection
- Menopause
- Anxiety
- Endocrine
    - Hyperthyroid
    - Nocturnal hypoglycaemia in diabetes
    - Acromegaly
    - Phaechromocytoma
- Obstructive sleep apnoea
- Connective tissue disease
- Neurological
    - Parkinsonism
    - Neuropathies
- Medications
    - Antipsychotics
    - SSRIs
    - Tramadol
    - Hormonal agents i.e. tamoxifen or GNRH analogues
    - Alcohol XS or withdrawal
    - Drug abuse
- Haematological malignancies

Suggested tests in primary care

- Clinical examination for lymph nodes &/or splenomegaly
- FBC
- Blood film (please request in additional test box)
- LDH, ESR and CRP
- TFTs
- Glucose
- Viral serology for EBV / CMV / HIV / Hepatitis B and C if relevant history
- Immunoglobulins
- Gonadotrophins
- CXR

Criteria for referral (Out-patient assessment)

- Significant additional systemic symptoms such as unexplained weight loss / fever / alcohol induced pain
- Associated lymphadenopathy and / or splenomegaly
- Abnormal FBC (please discuss with haematologist to see if possibly related and therefore, referral warranted)

Who does not need referral?

- Night sweats only, otherwise well with a normal FBC

13. SPLENOMEGALY

Palpable spleen or an enlarged spleen detected by imaging.

Causes include infections (viral, bacterial, parasitic), chronic liver disease, connective tissue disease, Gaucher's and sarcoidosis.

Haematological disorders associated with an enlarged spleen include autoimmune haemolytic anaemia, hereditary spherocytosis, myeloproliferative disorders, myelofibrosis, leukaemia and lymphoma.

Suggested tests in primary care

- FBC
- Blood film (please request in additional test box)
- ESR and CRP
- Reticulocyte count. If increased check a direct antiglobulin test (DAT) (pink transfusion EDTA tube on transfusion form)
- LFTs, GGT, AST, LDH
- Viral serology for EBV / HIV and hepatitis viruses
- Immunoglobulins + serum electrophoresis

Criteria for referral (Out-patient assessment)

- Significant systemic symptoms such as unexplained weight loss, sweats or fever
- Lymphadenopathy
- Evidence of haemolysis (raised reticulocyte count, LDH, bilirubin)
- Abnormal FBC (cytopenias, lymphocytosis or leucoerythroblastic film)

Who does not require referral?

- Chronic liver disease and portal hypertension (consider GI referral)
- Rheumatoid / Felty's / SLE – consider rheumatology referral

Before referral, consider discussing the imaging result with the duty Haematologist – this allows MDT review in conjunction with radiology in the first instance and determine whether outpatient review is required. Many patients reported to have mild splenomegaly (and no other concerning features or abnormal FBC) are due to body habitus.

14. LYMPHADENOPATHY

Can occur in a range of reactive, infective or neoplastic conditions and can be isolated or generalised.

Isolated lymphadenopathy usually results from local infection or neoplasm. Generalised lymphadenopathy may result from systemic infection or neoplasm.

Causes of lymphadenopathy

Infective	Bacterial	Tonsillitis, cellulitis, TB, syphilis, dental infection
	Viral	EBV, CMV, rubella, HIV, HBV, HCV, measles
	Other	Toxoplasma, histoplasmosis, Chlamydia, cat-scratch
Neoplastic	Haematological	Hodgkin's disease, NHL, CLL, ALL
	Others	Metastatic carcinoma
Collagen and other systemic disorders		Rheumatoid arthritis Sarcoidosis SLE Eczema

Suggested tests in primary care

- FBC
- Blood film (please request test in additional test box)
- ESR and CRP
- U+E, LFTs, LDH
- Viral serology for EBV / HIV / hepatitis B and C if relevant history
- CxR
- **referral for ultrasound of nodes – this can be useful for determining whether they are reactive or suspicious**
- **Refer to appropriate specialty for node biopsy***

*Haematology does not offer a biopsy service for tissue diagnosis and therefore referral to a specialty which can do this will speed up the diagnostic process and should occur in the first instance, e.g.:

- Neck nodes directed to ENT
- Axillary nodes directed to breast team
- Inguinal nodes directed to general surgery

Bone marrow examination should be reserved for staging in confirmed lymphoma or leukaemia cases – it is not commonly a useful primary investigation of lympadenopathy.

Criteria for haematology referral (Out-patient assessment)

- In association with splenomegaly
- Abnormal FBC (cytopenias, lymphocytosis or leucoerythroblastic film)

15. RAISED SERUM FERRITIN AND HAEMOCHROMATOSIS

A raised serum ferritin can be due to multiple differentia aetiologies including iron overload, inflammation, liver or renal disease, connective tissue disorders, malignancy and chronic alcohol consumption.
Ferritin levels are age and sex dependent.

Suggested first-line investigations in primary care of a raised serum ferritin are:

- FBC (+/- film if abnormal)
- Repeat serum ferritin (note laboratory will only repeat this after 30 days)
- Iron studies (transferrin saturation – ideally fasted)
- Inflammatory markers (ESR and CRP)
- U+E's
- LFT's including AST and GGT
- BBV serology
- Consider abdominal ultrasound

If transferrin saturation is > 50%, then a sample should be sent for HFE genotype (EDTA sample).

Markedly elevated serum ferritin levels (>10 000 µg/l) should prompt consideration of rare conditions, such as adult onset Still disease or haemophagocytic lymphohistiocytosis, but may also be seen in commoner conditions, such as renal or liver disease, infections and malignancies.

Criteria for referral (out-patient assessment)

- Confirmed genetic haemochromatosis – note if LFTs are abnormal or ferritin is > 1000mcg/L, this referral should be sent directly to gastroenterology
- Elevated serum ferritin + transferrin saturation secondary to iron overload (excessive intake or supplementation, or transfusion)
- Elevated serum ferritin + transferrin saturation + abnormal FBC as this may indicate a myelodysplastic syndrome or iron-loading anaemia

Who does not need haematology referral?

- Haemochromatosis carriers
- Isolated raised serum ferritin: in otherwise well patients with unexplained and moderately elevated serum ferritin levels (<1000 µg/l) and normal transferrin saturation, a period of observation, with lifestyle adjustment if appropriate, may be reasonable with repeat assessment after 3–6 months. Patients with unexplained persistent hyperferritinaemia (especially >1000 µg/l) require referral to gastroenterology.

16. Thrombophilia

Thrombophilia testing is not generally useful as a predictive tool in patients after a blood clot and therefore neither a negative test nor a positive test alters management. There are therefore few indications for testing.

Children with purpura fulminans – for protein C/S deficiency
Adults with skin necrosis
Pregnant women considered at high risk of thrombosis

GPs and other consultants should discuss whether a thrombophilia screen is indicated on all other cases with duty haematologist.

Note

1. Testing should be delayed 6 weeks in patients who have had a venous thrombosis
2. There should be at least a 4 week gap between cessation of warfarin therapy and thrombophilia testing
3. Patients on oral, subcutaneous or intravenous anticoagulation should not be tested
4. Patients who are pregnant or taking an oestrogen based medication should not be tested unless discussed with haematology
5. Any questions regarding thrombophilia should be discussed with the duty haematologist

Sample requirements

3 x Sodium Citrate bottle (light blue cap) + 1 x yellow topped bottle

D-Dimers

D-dimer testing is not offered in the community for the purpose of excluding PTE or DVT.

17. Easy bruising

Easy bruising is a common referral and a primary haematological cause is rarely found. It is frequent in the elderly (senile purpura). Excessive bruising may be a manifestation of a vascular defect (steroid use, uraemia, scurvy, collagen disease, paraproteinaemia) rather than a coagulopathy or platelet disorder.

Consider:

- Site / extent / associated with trauma / painful
- Associated symptoms e.g. epistaxis, menorrhagia, bleeding after skin trauma / dental extraction / post-partum
- Family history
- Drugs – NSAIDs, anti-platelet agents, anticoagulants, SSRIs, ibrutinib
- Systemic enquiry – hepatic and renal failure will cause a haemorrhagic tendency, are there signs of a connective tissue disorder

Screening tests

- FBC, coagulation screen
- U+E, LFTs