Title	**GP Adult Haematology Guidelines**
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1. Introduction

This document is designed to help general practitioners with routine haematological problems. It may also be useful to guide hospital doctors in the further investigation of abnormal haematological parameters.

2. Guideline Scope

These guidelines do not apply to children or patients who are pregnant.

It is difficult to give advice for every clinical situation as all patients are different. Further monitoring or investigation may not be appropriate in some patient groups. Likewise, patients may present with multiple different abnormalities and therefore further advice may be required.

Where major abnormalities are found on the blood film that require urgent attention e.g. acute leukaemia, microangiopathic haemolytic anaemia, platelet count less than 10×10^9/L etc. we will contact a general practitioner directly. When a blood film or coagulation screen is reviewed by a haematologist there may be specific suggestions made to guide referral or further investigations.

As pre-analytical variables can play a part in abnormal results we suggest repeating a sample if an unexpected result is encountered. Frequently our advice is based on the pattern of abnormalities and how these have developed and therefore reviewing older blood tests is useful to guide further management.

If we have advised you to perform a blood film please request this with relevant clinical details and request for 'medical review as per consultant haematologist'.

The laboratory is often able to add on tests to existing samples but this is only usually possible if done within 48 hours. Please see https://www.newcastle-hospitals.nhs.uk/services/laboratory-medicine/ for full details on our testing repertoire and how to request add on tests. If you send us an Advice and Guidance request within this time frame it often allows us to request more advanced tests and therefore advances patient management more quickly.

3. Useful resources:

- British Society for Haematology Guidelines: https://b-s-h.org.uk/guidelines
- Newcastle Laboratories. https://www.newcastle-hospitals.nhs.uk/services/laboratory-medicine/
- Newcastle upon Tyne Hospitals NHS Foundation Trust clinical haematology services https://www.newcastle-hospitals.nhs.uk/services/haematology/
- Applications: Buku Medicine – all you need to know about haematology with GPs in mind – free to download on IOS and Android

4. Contacting the Haematology service

If advice is required about a haematological problem this should usually be via the Advice and Guidance service in the first instance. If help is required with a patient that is currently under our care or previously known to our service then please write to the appropriate haematologist directly. We are not able to offer advice on patients where their blood tests are analysed at a different laboratory. We suggest discussing with a local haematologist in this instance. We aim to reply to all GP Advice and Guidance requests within two working days but an answer will often come sooner. If you need urgent or emergency advice that cannot wait then please contact the on call haematology registrar via switchboard.

5. Evaluation and feedback

This guideline has been prepared by Dr Andrew McGregor, consultant haematologist. It has been reviewed by Dr Tina Biss, Dr Brigit Greystoke, Dr Erin Hurst, Dr Gail Jones, Professor Steve O'Brien, Dr Wendy Osborne and Dr Kate Talks. Any feedback please contact Dr McGregor via NHS.net global address book or via Blood Sciences department: tnu-tr.NewcastleLaboratories@nhs.net (this is not for clinical queries).

6. Document changes

Any document changes must be updated in:

- NCCC Q Pulse
- Laboratory medicine Q Pulse
- Trust website (haematology departmental website and Newcastle Laboratories)
- Intranet
- GP TeamNet

Contents

Anaemia

The haemoglobin concentration reference range for men is 130-180 g/L and women is 115-165 g/L. The cause of anaemia can generally be separated by the MCV – see separate sections on microcytosis or macrocytosis. However the MCV is not completely sensitive or specific and there may be more than one cause of anaemia occurring together so detailed investigation is often required.

Causes

- Iron deficiency and bleeding
- Anaemia of chronic disease/inflammation
- Malignancy including myeloma
- Renal failure especially if eGFR less than 30 ml/min or associated with diabetes
- Alcohol and liver disease
- Vitamin B12 or folate deficiency
- Haemolysis; including drug-induced
- Medications especially chemotherapy, anti-androgens and immunomodulatory drugs – check British National Formulary (BNF)
- Pregnancy
- Testosterone deficiency
- Thyroid dysfunction
- Thalassaemia and haemoglobinopathy
- Bone marrow failure e.g. aplastic anaemia, myelodysplastic neoplasm
- Bone marrow infiltration e.g. leukaemia, non-haematological cancer

History and examination

Look at causes and work through systematically. Look at older blood counts.

Suggested investigations

See pages on microcytosis and macrocytosis. If the anaemia is normocytic then all causes should be excluded.

- Check inflammatory markers
- Renal and liver function
- Immunoglobulins
- In elderly men where no clear cause of anaemia the endocrinology team have suggested: “9am fasting testosterone, free testosterone, sex hormone binding globulin, LH, FSH and request endocrine advice on interpreting results.”

Management

This depends on the underlying cause. If the above causes have been excluded, then the most likely explanations are anaemia of chronic disease or a bone marrow failure syndrome. The latter is frequently associated with other cytopenia or changes on the blood film. In patients with otherwise normal full blood count and for whom there are no concerning features we suggest monitoring the full blood count in general practice. In anaemia of chronic disease, the treatment is of the underlying cause and if concerns then a referral to the appropriate speciality should be made. Chronic diseases associated with anaemia include inflammatory diseases, diabetes, heart failure and COPD. For cases of renal anaemia refer to nephrology. If there is haemolysis or concerns about myelodysplastic neoplasm, then a discussion with haematology is required.

If there is no evidence of inflammation, please consider discussing with haematology if the haemoglobin is persistently less than 110 g/L in men or less than 100 g/L in women for evaluation into possible myelodysplastic neoplasm. If there is uncertainty of whether referral is required especially when the haemoglobin concentration is greater than 100 g/L please discuss via Advice and Guidance. If the patient is not referred to haematology then continued monitoring for any changes is likely to be appropriate.

Polycythaemia

The haemoglobin reference range for men is 130-180 g/L and women is 115-165 g/L. The haematocrit for men is 0.4-0.5 L/L and women is 0.36-0.46 L/L. Polycythaemia is usually a secondary phenomenon due to reduced plasma volume or respiratory disease. Polycythaemia vera is a clonal myeloproliferative neoplasm. Around 96% of patients with primary polycythaemia will have the *JAK2* V617F mutation and a further 1-2% will have mutations in *JAK2* exon 12. Patients with primary polycythaemia vera may have iron deficiency due to increased demand. In this scenario red cell indices may show a normal or high haemoglobin with an elevated haematocrit and elevated RBC but low MCV. This pattern is unique to iron deficient polycythaemia. Please do not give iron in this setting as this will further increase the haemoglobin concentration.

Causes

Apparent or relative or pseudo polycythaemia – reduction in plasma volume	**Absolute or true polycythaemia – increase in red cell mass**
Alcohol	Secondary polycythaemia
Diuretics	• Chronic lung disease and hypoxia
Dehydration	• Cyanotic heart disease
SGLT2 inhibitors e.g. dapagliflozin	• High altitude
	• Smoking
	• Sleep apnoea
	• Abnormal erythropoietin production
	○ Local hypoxia e.g. polycystic kidneys, renal artery stenosis
	○ Erythropoietin-producing tumour e.g. HCC, RCC, fibroids
	• Renal transplant
	• Drugs e.g. erythropoietin, testosterone, anabolic steroids
	Polycythaemia vera
	Inherited disorders e.g. high affinity oxygen haemoglobin
	Idiopathic

History and examination

This should focus on the more common causes – relative polycythaemia and secondary polycythaemia. Look at medications – especially diuretics, take an alcohol and smoking history and ask about respiratory symptoms. Ask about any illicit drugs or over the counter medications. Measure oxygen saturations and blood pressure. Ask about B symptoms, rashes, itch, aquagenic pruritus, erythromelalgia, gout, bleeding, thrombosis and examine for splenomegaly and plethora. Ask about symptoms of hyperviscosity e.g. headaches and visual disturbances. Look at older blood counts.

Suggested investigations

- Blood film
- Renal and liver function
- Calcium
- Ferritin
- *JAK2* mutation – available in primary care (please only request on advice of haematology)
- Erythropoietin level – available in primary care (please only request on advice of haematology)
- Chest radiograph if respiratory issues

Management

- If the haematocrit or haemoglobin are only mildly elevated it is reasonable to offer lifestyle advice and repeat the test in four months.
- If any secondary causes are apparent these should be treated or modified accordingly (e.g. smoking cessation, stopping diuretics, optimising lung disease, alcohol cessation etc.).
- If there is an elevation in haematocrit or haemoglobin associated with a thrombotic event or symptoms of hyperviscosity then there should be a referral to or discussion with haematology
- If the patient is hypoxic due to respiratory or cardiovascular diseases then advice should be sought from the appropriate specialist.
- If there is clinical suspicion of primary polycythaemia (constitutional symptoms, splenomegaly, no other secondary cause and persistent) please refer to haematology
- If secondary polycythaemia seems likely but primary polycythaemia needs to be excluded please discuss via Advice and Guidance for *JAK2* testing which is available in primary care
- If the patient has the *JAK2* mutation please refer to haematology as this is indicative of a myeloproliferative neoplasm
- Please refer to haematology if the haematocrit is persistently (three months apart) above 0.52 L/L in men and 0.48 L/L in women and no secondary cause. If the haematocrit does not reach these thresholds and the MCV or ferritin is low please discuss with Advice and Guidance as this could be iron deficient polycythaemia vera.
- Do not give iron therapy to patients who are iron deficient but have an elevated haematocrit – discuss with Advice and Guidance.
- If the haemoglobin concentration or haematocrit is very high (e.g. haematocrit over 0.6 L/L in men and 0.56 L/L in women) or there are symptoms of hyperviscosity please discuss or refer urgently.
- Cardiovascular risk factors (including hyperlipidaemia, hypertension and diabetes) should be managed for all patients with polycythaemia of any cause

References

- NICE Clinical Knowledge Summary. Polycythaemia / Erythrocytosis (September 2024). https://cks.nice.org.uk/topics/polycythaemia-erythrocytosis/
- McMullin MF, Mead AJ, Ali S, *et al*. A guideline for the management of specific situations in polycythaemia vera and secondary erythrocytosis: A British Society for Haematology Guideline. *Br J Haematol* 2019; **184**: 161-175. https://b-s-h.org.uk/guidelines/guidelines/management-of-specific-situations-in-polycythaemia-vera-and-secondary-erythrocytosis/
- McMullin MF, Harrison CN, Ali S, *et al*. A guideline for the diagnosis and management of polycythaemia vera. A British Society for Haematology Guideline. *Br J Haematol* 2019; **184**: 176-191. https://b-s-h.org.uk/guidelines/guidelines/diagnosis-and-management-of-polycythaemia-vera/

Macrocytosis

The normal MCV depends on age but is generally 83-101 fL. This can be present with or without anaemia.

Causes

- Artefact e.g. delay to analysis
- Alcohol and liver disease
- Vitamin B12 or folate deficiency
- Haemolysis (due to reticulocytosis)
- Medications especially hydroxycarbamide, methotrexate, chemotherapy and other immunomodulatory drugs
- Paraprotein
- Pregnancy
- Thyroid dysfunction
- Myelodysplastic neoplasm and aplastic anaemia – often associated with neutropenia and/or thrombocytopenia

History and examination

Suggest looking at the above causes and look for signs of liver disease. Review older blood tests. Ask about diet and malabsorption.

Suggested investigations

- Liver function tests
- Vitamin B12 and folate
- Blood film
- Haemolysis screen (reticulocytes, blood film, direct antiglobulin test, lactate dehydrogenase, haptoglobin)
- Pregnancy test
- Immunoglobulins and serum protein electrophoresis
- TSH

Management

- Correct any secondary cause and consider repeating test in first instance
- If haemolysis is suspected then please discuss
- If myelodysplastic neoplasm is suspected (other cytopenias or blood film abnormalities) then please discuss
- Please discuss cases with macrocytic anaemia when the haemoglobin is persistently less than 110 g/L in men or less than 100 g/L in women and there are no secondary causes.
- If the MCV is high with no anaemia or other cytopenia and no cause is identified then these patients can be monitored in primary care every six to 12 months
- If patient has liver disease please discuss with hepatology
- If a paraprotein is detected please see separate guideline on this

Microcytosis

The normal MCV depends on age but generally 83-101 fL.

Causes

- Iron deficiency
- Thalassaemia and haemoglobinopathy
- Anaemia of chronic disease
- Lead poisoning (rare)
- Inherited sideroblastic anaemia (rare)

History and examination

Look for signs of anaemia. Ask about diet, weight loss and potential blood loss. Review older blood tests.

This table can help differentiate between iron deficiency and thalassaemia (trait).

Factor	Iron deficiency	Thalassaemia (trait)
Haemoglobin	Low or normal	Low or normal
MCV/MCH	Low but can be normal	Low – often lower than would expect from haemoglobin concentration
RBC	Low or normal	High
RDW	Elevated	Normal
Previous FBC	May be normal	Persistently low MCV/MCH
Family FBC	May be normal	If inherited may have similar abnormalities
Blood film	May be normal or may show hypochromia and pencil cells.	Depends on type
Ethnicity	Any	More common in certain ethnic groups

Suggested investigations

- Ferritin
- If suspect iron deficiency and serum ferritin is normal check inflammatory markers (e.g. CRP) as inflammation may elevate ferritin into the normal range. In this case a blood film, reticulocyte haemoglobin or transferrin saturation may be useful
- Haemoglobinopathy screen if suspected thalassaemia or haemoglobinopathy. Please see further section on haemoglobinopathy/thalassaemia.
- If lead poisoning is suspected please check serum lead level and blood film
- In some patients a trial of iron may be a diagnostic and therapeutic manoeuvre

Management

- We do not review patients with iron deficiency in haematology.
- See section on iron deficiency for more details.
- We do not routinely review patients with thalassaemia trait but happy to be contacted via Advice and Guidance if concerns or further questions. Please see further section on haemoglobinopathy/thalassaemia.

Thrombocytopenia

The normal platelet count is 150-450 × 10^9/L. It would be unusual to get bleeding symptoms with a platelet count above 50 × 10^9/L. Spontaneous bleeding is increased when the platelet count is below 30 × 10^9/L.

Causes

- Artefact e.g. platelet clumping
- Medications (including 'over the counter', herbal remedies) – check BNF
- Infections including viral (e.g. HIV, CMV, EBV and hepatitis) and *Helicobacter pylori*
- Liver disease and alcohol
- Hypersplenism
- Vitamin B12 or folate deficiency
- Autoimmune diseases
- Pregnancy
- Thyroid dysfunction
- Sepsis
- Major haemorrhage
- Disseminated intravascular coagulation
- Immune thrombocytopenia (ITP)
- Anti-phospholipid syndrome
- Inherited bleeding disorders
- Thrombotic thrombocytopenic purpura
- Bone marrow failure e.g. myelodysplastic neoplasm or aplastic anaemia
- Bone marrow infiltration e.g. acute leukaemia
- Post-transfusion purpura

History and examination

Think about asking questions to rule out above causes. Ask about bleeding symptoms, alcohol and a family history. Examine for hepatosplenomegaly, signs of liver disease, signs of autoimmune disease and any bruises. Review older blood tests and take a medication history.

Suggested investigations

These may depend on the history and examination.

- Blood film
- Vitamin B12 and folate
- Liver function tests and TSH
- HIV, hepatitis B and C
- Coagulation screen
- Pregnancy test
- Consider autoimmune screen if history or examination suggestive
- Abdominal ultrasound if concerned about liver disease or palpable splenomegaly

Management

- Repeat the FBC to exclude artefact, unless symptomatic, when urgent assessment is required.
- Asymptomatic patients with a stable platelet count >80 × 10^9/L should be assessed for secondary causes and do not usually require haematology review. Repeat the FBC in 4 to 6 weeks; if stable, monitor every 4 months for 12 months, then annually. Monitoring can usually stop after 12 months of stability, but patients should report bleeding symptoms and have an FBC before procedures.
- Refer or discuss if there is another cytopenia, a blood film abnormality, or concern about haematological malignancy.
- Refer to haematology if the platelet count is <80 × 10^9/L for more than 4 months or in patients awaiting surgery.
- If the platelet count is <50 × 10^9/L or there are bleeding symptoms, arrange an urgent repeat FBC and referral.
- Antiplatelet and anticoagulant therapy are generally avoided when platelets are <50 × 10^9/L and are usually safe when >100 × 10^9/L. Between 50 and 100 × 10^9/L, treatment decisions should be individualised according to bleeding and thrombotic risk.
- If thrombocytopenia is due to liver disease, discuss with hepatology.

Thrombocytosis

Thrombocytosis is defined as a platelet count over 450 × 10^9/L. This is frequently a reactive transient problem relating to infection or inflammation. If persistent it may represent a myeloproliferative neoplasm. In patients with myeloproliferative neoplasms there is an increased risk of thrombosis but also bleeding if the platelet count is very high e.g. over 1500 × 10^9/L.

Causes

- Infection
- Inflammation e.g. autoimmune disease, solid organ malignancy, trauma
- Bleeding
- Iron deficiency
- Hyposplenism
- Medications e.g. rebound post chemotherapy and thrombopoietin agonists
- Spurious e.g. bacteria, fragments, cryoglobulin
- Myeloproliferative neoplasms e.g. essential thrombocythaemia, chronic myeloid leukaemia, polycythaemia vera, myelofibrosis

History and examination

This should focus on ruling out the above causes. Review older blood tests. Look for splenomegaly and for features of autoimmune disease. Ask about itch, bleeding, rashes, sweats and weight loss. Ensure that there has been no prior splenectomy. Ask about risk factors for iron deficiency or other malignancy.

Suggested investigations

- Liver function tests
- Calcium
- Inflammatory markers
- Ferritin
- Blood film

Management

- Refer to haematology if platelet count over 800 × 10^9/L with no reactive cause
- If platelet count 450-800 × 10^9/L then suggest repeat the blood count in four to six weeks in first instance or discuss with the Advice and Guidance team if clinical concerns, high thrombosis risk, aged over 60 or constitutional symptoms/splenomegaly.
- If the platelet count is persistently above 450 × 10^9/L with no secondary cause for over four months then suggest referral to haematology.
- If there is a history of thrombosis or bleeding or the platelet count is over 1000 × 10^9/L this is likely to require more urgent referral

References

- NICE Clinical Knowledge Summary December 2025. How should I assess a person with thrombocytosis? https://cks.nice.org.uk/topics/platelets-abnormal-counts-cancer/diagnosis/assessment-of-thrombocytosis/
- Harrison CN, Butt N, Campbell P, *et al*. Diagnostic pathway for the investigation of thrombocytosis. *Br J Haematol* 2013; **161**: 604-606. British Journal of Haematology | Wiley Online Library
- Harrison CN, Bareford D, Butt N, *et al*. Guideline for investigation and management of adults and children presenting with a thrombocytosis. *Br J Haematol* 2010; **149**: 352-375. British Journal of Haematology | Wiley Online Library

Neutropenia

A normal neutrophil count is 2-7 × 10^9/L and neutropenia is defined if the neutrophil count is less than 1.5 × 10^9/L. Mild neutropenia is 1-1.5 × 10^9/L, moderate neutropenia is 0.5-0.99 × 10^9/L and severe neutropenia is less than 0.49 × 10^9/L. Patients are at risk of more serious infection when the neutrophil count falls below 1 × 10^9/L and especially when less than 0.5 × 10^9/L.

Causes

- Medications – check BNF
- Viral infections
- Autoimmune disease
- Vitamin B12 or folate deficiency
- Sepsis
- Duffy null-associated neutropenia (see box)
- Hypersplenism
- Felty syndrome
- Thyroid dysfunction
- Nutritional deficiencies e.g. anorexia nervosa
- Bone marrow failure disorders e.g. myelodysplastic neoplasm, aplastic anaemia
- Bone marrow infiltration e.g. acute leukaemia, T-cell large granular lymphocytic leukaemia
- Congenital syndromes e.g. cyclical neutropenia

Duffy null-associated neutropenia (previously known as benign ethnic neutropenia) results in the loss of the Duffy antigen on cells and is common among populations of African and Middle Eastern ancestry due to the evolutionary advantage of protection against *Plasmodium vivax* infection. Despite the average lower neutrophil count of 0.7-1.2 × 10^9/L there is no increased risk of infection and people show a normal neutrophil response when required. Although Duffy antigen testing is available this diagnosis can frequently be made clinically based on persistent mild neutropenia, lack of infections and no clear secondary cause in a person with a background where the Duffy null status is common.

History and examination

Ask about the above causes, recurrent infections, mouth ulcers and family history. Examine for signs of autoimmune disease, liver disease and lymphadenopathy and splenomegaly. Review older blood tests.

Suggested investigations

- Liver function tests
- HIV, hepatitis B and C
- Blood film
- TSH
- Vitamin B12 and folate
- Ferritin
- Autoimmune screen if history or examination suggestive

Management

The management will vary from patient to patient depending on differential diagnosis, prior blood counts and clinical concern. Causative medications may not need to be stopped if they are important and the neutrophil count is above 1 × 10^9/L and there are no recurrent infections. In neutropenia associated with viral infections this may persist for weeks and less commonly for a few months.

In general

- Neutrophil count 1.5 × 10^9/L and above – rule out secondary causes as per suggested history, examination and investigations. Repeat in four weeks' time and if stable and no concerns then no further investigation.
- Neutrophil count 1-1.49 × 10^9/L – rule out secondary causes as per suggested history, examination and investigations. Repeat in two to four weeks' time and if still low seek advice through Advice and Guidance service for specific management plan. If there are no associated full blood count

abnormalities, film abnormalities or clinical concern patients can usually be monitored in primary care

- Neutrophil count below 1×10^9/L. A blood film will have been performed in these situations and the results can guide frequency and timing of further tests. In general, someone with a neutrophil count persistently below 1×10^9/L after a repeat in two weeks needs haematological assessment.
- If the neutropenia is associated with other blood count or film abnormalities or abnormalities on examination or recurrent infections then make a formal referral
- If the patient is of Black African or Middle-Eastern ethnicity then a neutrophil count is commonly 0.8-2 $\times 10^9$/L with no clinical consequence. This is a diagnosis of exclusion after ruling out other causes and seeing a persistent low count without increased risk of infection. Please perform the above investigations and if normal and the neutrophil count remains above 1×10^9/L then no further investigation is required.
- If a patient with a neutrophil count less than 1×10^9/L presents with fever or with clinical signs of sepsis they should be admitted and treated with intravenous antibiotics as per the policy for neutropenic sepsis

Neutrophilia

This is usually a reactive phenomenon and only rarely will represent a primary haematological malignancy. It is unusual for a reactive neutrophilia to be above 100 × 10^9/L. The finding of basophilia points towards a myeloproliferative neoplasm; especially chronic myeloid leukaemia. If there is an associated monocytosis which is persistent see section on monocytosis.

Causes

- Infection – especially bacterial
- Smoking
- Medications e.g. corticosteroids, GCSF, lithium
- Stress events e.g. trauma, seizures, myocardial infarction, eclampsia etc.
- Autoimmune diseases or other inflammatory processes
- Malignancy (haematological or solid tumour)
- Hyposplenism
- Myeloproliferative neoplasms such as chronic myeloid leukaemia, myelofibrosis and chronic neutrophilic leukaemia (these conditions are often identified or suspected on the blood film)

History and examination

Careful clinical evaluation asking about infective symptoms, travel history, smoking history and into the above causes. Examine for features of autoimmune disease, lymphadenopathy and splenomegaly. Review older blood tests.

Suggested investigations

- CRP
- Blood film
- Dependant on history and examination

Management

The management will vary from patient to patient depending on differential diagnosis, prior blood counts, result on repeat and clinical concern.

- If persistent basophilia suggest referral or discussion via Advice and Guidance
- If neutrophil count persistently above 20 × 10^9/L without a reactive cause suggest referral
- If there is neutrophilia and splenomegaly or blood film abnormalities then suggest referral
- If unexplained inflammatory process suggest refer to general medicine depending on localising features

Lymphopenia

The reference range depends on age but in adults is 1.5-4.5 × 10^9/L.

Causes

- Acute infections especially bacterial
- Chronic infections e.g. tuberculosis
- HIV
- Increasing age
- Medications e.g. steroids
- Autoimmune diseases
- Chronic diseases e.g. cardiac failure, renal failure
- Congenital immunodeficiency syndromes
- Lymphoma

History and examination

Look to exclude the above causes. Examination for lymphadenopathy and ask about B symptoms and recurrent infections. Look for symptoms or signs of autoimmune disease. Review older blood tests.

Suggested investigations

- HIV test

Management

- If the lymphopenia is persistent with no secondary causes and no clinical concerns then no further action is required
- It would be extremely unusual for a patient to have lymphopenia as the sole presenting feature of lymphoma however if there are other clinical concerns e.g. lymphadenopathy, B symptoms then please refer.
- If the patient has recurrent infections and is lymphopenic (and HIV negative) then suggest check immunoglobulins and discuss with immunology

Lymphocytosis

The reference range depends on age but in adults is 1-5-4.5 × 10^9/L. In younger patients lymphocytosis is often reactive but this is less common in the elderly where a malignant disorder is more likely.

Causes

- Viral infection
- Tuberculosis and pertussis
- Hyposplenism
- Smoking
- Stress response e.g. post myocardial infarction
- Non-Hodgkin lymphoma e.g. chronic lymphocytic leukaemia

History and examination

Review older blood tests. Ask about recent viral infections. Ask about weight loss, B symptoms, recurrent infections and smoking. Examine for lymphadenopathy and hepatosplenomegaly.

Suggested investigations

- Blood film
- Monospot if EBV suspected

Management

- Repeat the full blood count in 4 to 6 weeks to assess for resolution, particularly following a viral infection.
- Refer if lymphocytosis persists and is associated with recurrent infections, B symptoms, lymphadenopathy, hepatosplenomegaly, other cytopenia, or concerning blood film features.
- In older adults, persistent lymphocytosis is often due to a lymphoproliferative neoplasm, most commonly chronic lymphocytic leukaemia (CLL). As early treatment offers no benefit in asymptomatic patients, formal diagnosis may not be needed in those with mild lymphocytosis.
- If the lymphocyte count is persistently >10 × 10^9/L, consider Advice and Guidance. If persistently >20 × 10^9/L, refer to haematology.

Patients diagnosed with CLL on immunophenotyping do not necessarily require haematology follow-up. Primary care monitoring is usually appropriate if all of the following apply:

- No B symptoms
- No or minimal lymphadenopathy
- Normal haemoglobin, platelet and neutrophil counts
- Stable lymphocyte count ≤30 × 10^9/L

Monitor at 3 months, then 6-monthly for 2 years, and annually thereafter if stable.

Re-refer to haematology if:

- Falling haemoglobin, platelet count or neutrophil count without another explanation
- Progressive lymphadenopathy or splenomegaly
- Development of B symptoms
- Significant patient anxiety

If uncertain, please discuss via Advice and Guidance.

References

- Bloodwise patient information (CLL). https://bloodcancer.org.uk/understanding-blood-cancer/leukaemia/chronic-lymphocytic-leukaemia-cll/
- Macmillan patient information (CLL). https://www.macmillan.org.uk/cancer-information-and-support/leukaemia/chronic-lymphocytic-leukaemia-cll

Eosinophilia

The normal eosinophil count is 0.04 to 0.4 × 10^9/L. Hypereosinophilia is an increased eosinophil count 1·5 × 10^9/L or greater persisting for at least six months for which no underlying cause can be found. It can be associated with signs of organ dysfunction (cardiac, respiratory, gastrointestinal and neurological).

Causes

- Atopy and/or allergy e.g. asthma, eczema
- Infections – parasites, fungal, HIV
- Medications – ACE inhibitors, penicillin, anti-epileptics, PPI – check BNF
- Autoimmune
    - Eosinophilic granulomatosis with polyangitis
    - Polyarteritis nodosa
    - SLE
    - Idiopathic eosinophilic synovitis
    - Eosinophilic fasciitis
    - Rheumatoid arthritis
- Respiratory
    - Allergic broncho-pulmonary aspergillosis
    - Asthma
    - Sarcoidosis
    - Löffler syndrome
    - Eosinophilic pneumonia
- Dermatological
    - Wells syndrome
    - Pemphigoid
    - DRESS syndrome
- Gastrointestinal
    - Chronic pancreatitis
    - Inflammatory bowel disease
    - Coeliac disease
- Dialysis
- Malignant disorders
    - Solid organ tumour
    - Hodgkin lymphoma
    - T-cell non-Hodgkin lymphoma
    - Mastocytosis
    - Malignant eosinophilic disorders

History and examination

There is such a wide variety of differentials that a systematic approach is required. Travel history is important. Look at older blood counts.

Suggested investigations

- Blood film
- Inflammatory markers
- Renal and liver function
- Calcium
- Stool ova cysts and parasites and others as guided by history e.g. strongyloides
- Coeliac screen
- Autoimmune screen and ANCA
- IgE
- Chest radiograph if respiratory features

Management

Please refer urgently if:

- Eosinophil count over 10 × 10^9/L without an obvious secondary cause
- Eosinophil count over 1.5 × 10^9/L with end organ damage or suspected haematological malignancy

A routine referral can be made if the eosinophil count is persistently over 1.5 × 10^9/L and no secondary cause has been found. Eosinophilia related to clear secondary causes e.g. respiratory disease, autoimmune disease is not routinely reviewed by haematology

References

Butt NM, Lambert J, Ali S, *et al*. Guideline for the investigation and management of eosinophilia. *Br J Haematol* 2017; **176**: 553-572.
https://b-s-h.org.uk/guidelines/guidelines/investigation-and-management-of-eosinophilia/

Basophilia

The normal reference range is 0-0.1 × 10^9/L. There are very few causes of basophilia and if this is persistent – particularly if above 0.4 × 10^9/L this is strongly suggestive of a myeloproliferative neoplasm.

Causes

- Chronic myeloid leukaemia
- Other myeloproliferative neoplasms e.g. myelofibrosis
- Atypical chronic myeloid leukaemia (MDS/MPN with neutrophilia)
- Ulcerative colitis
- Hypothyroidism
- Recovery from acute illness
- Allergy
- Chicken pox
- Hyposplenism

History and examination

Look for signs of infection including atypical infections. Examine for splenomegaly and hepatomegaly. Ask about weight loss, and night sweats. Look at older blood counts.

Suggested investigations

- Blood film
- Inflammatory markers
- TSH

Management

Basophilia is seldom seen in reactive states save for very mild elevations e.g. 0.2 × 10^9/L. If the basophil count is elevated it should be repeated in three to four weeks to see if persistent and a blood film should be requested. If the basophilia is persistent then please discuss via Advice and Guidance. If a blood film is reported as concerning for chronic myeloid leukaemia or a myeloproliferative neoplasm please refer directly to haematology.

Monocytosis

The normal reference range is 0.2-0.8 × 10^9/L and monocytosis is frequently transient.

Causes

- Infections e.g. tuberculosis, brucella, malaria, syphilis, endocarditis
- Autoimmune and inflammatory diseases
- Stress response e.g. post myocardial infarction
- Sarcoidosis
- Hyposplenism
- Chronic myelomonocytic leukaemia
- Malignancy

History and examination

Look for signs of infection including atypical infections. Ask about a travel history. Examine for splenomegaly and hepatomegaly. Ask about weight loss, rashes and night sweats. Look at older blood counts.

Suggested investigations

- Blood film
- Inflammatory markers
- Renal and liver function
- Calcium

Management

If the monocytosis is persistent this may represent chronic myelomonocytic leukaemia. This is a chronic and generally incurable disorder. Some cases behave indolently and others can be more aggressive. Suggest referral if:

- Persistent monocyte count over 5 × 10^9/L
- Monocyte count over 1.2 × 10^9/L with other cytopenia or concerning symptoms or abnormal features on blood film

If the monocyte count is between 1.2 and 5 × 10^9/L with no other cytopenia and no constitutional symptoms or splenomegaly then please discuss via Advice and Guidance and monitor every six to 12 months.

Paraprotein

There is a separate guideline on this located on the Newcastle Haematology website: https://www.newcastle-hospitals.nhs.uk/services/haematology/gp-advice-and-guidance/ and also on Q Pulse NUTH_0062

Splenomegaly

The size of the spleen is determined by sex, age and height. We recommend using this calculator to determine the expected spleen size: https://qxmd.com/calculate/calculator_384/expected-spleen-size. Mild splenomegaly (14 cm or less) is usually not concerning.

Causes

- Liver disease with portal hypertension
- Viral infection e.g. EBV, CMV
- Other infections e.g. tuberculosis, infective endocarditis, tropical diseases, syphilis
- Autoimmune diseases e.g. rheumatoid arthritis
- Metabolic storage disorders e.g. Gaucher's disease
- Sarcoidosis
- Lymphoma
- Myeloproliferative neoplasms e.g. chronic myeloid leukaemia, myelofibrosis
- Haemolytic anaemias, thalassaemia and haemoglobinopathies

History and examination

Look at previous imaging if available. Ask about symptoms relating to spleen size e.g. pain, early satiety. Clinically evaluate for above causes including asking about B symptoms, recent viral infection, features of autoimmune disease, family history and travel history. Review any previous imaging.

Suggested investigations

- Full blood count and blood film
- Ultrasound scan of abdomen
- Liver function tests
- Viral screen e.g. EBV, CMV, HIV, hepatitis B and C
- Haemolysis screen (blood film, reticulocyte count, LDH, LFTs, haptoglobin, DAT)
- Immunoglobulins and serum protein electrophoresis
- Autoimmune screen if history suggestive
- Others depending on clinical history and examination and differential diagnosis

Management

- If spleen size is enlarged for height and sex but 14 cm or less and no other cause and no suspicion regarding haematological aetiology then suggest repeating ultrasound scan in four to six months to see if resolving and to ensure not increasing in size.
- If persistently enlarged over 14 cm or 2 cm above predicted or if concerns regarding haematological malignancy then suggest referral to haematology unless underlying liver disease or infective cause
- If underlying liver disease suggest discuss with gastroenterology in the first instance
- Discuss with Advice and Guidance team if concerns

Lymphadenopathy

Lymphadenopathy may occur in both benign and malignant conditions. Features suggestive of lymphoma include persistent, non-tender, progressive lymphadenopathy, particularly when associated with B symptoms (weight loss, drenching sweats or unexplained fever), pruritus or alcohol-induced nodal pain. A normal full blood count does not exclude lymphoma, and fluctuating lymph node size does not rule it out.

Causes

- Infections – particularly localised infection, tuberculosis, syphilis
- Post-vaccine
- Non-haematological malignancy
- Lymphoma or other haematological malignancy
- Sarcoidosis
- Skin conditions e.g. eczema
- Kikuchi disease

History and examination

To look at causes above. Ask about infections, itch, alcohol-induced pain, weight loss, sweats and fevers. A travel history may be informative. Systemic enquiry is required. Examination for splenomegaly and hepatomegaly as well as other lymph node areas. Ask about symptoms suggestive of superior vena cava obstruction or stridor.

Suggested investigations

- Full blood count and blood film (urgent)
- Inflammatory markers
- Renal, liver and bone profile
- LDH
- Immunoglobulins and serum protein electrophoresis
- HIV test
- Syphilis serology
- Monospot test if possible EBV and toxoplasma, CMV and EBV serology as appropriate
- Autoimmune screen if history is suggestive

Management

Please refer if:

- Lymphadenopathy is present for <6 weeks and is associated with B symptoms, hepatosplenomegaly, rapid nodal enlargement, generalized lymphadenopathy, anaemia, thrombocytopenia, hypercalcaemia or pruritus.
- Lymphadenopathy >1 cm persists for >6 weeks without an obvious infective cause.
- There is clinical suspicion of a haematological malignancy but the presentation is not clear-cut. In such cases, please discuss via Advice and Guidance.

Lymphoma diagnosis requires a lymph node biopsy. Where appropriate, direct referral to the relevant surgical specialty may expedite diagnosis (ENT for cervical nodes, breast surgery for axillary nodes, and general surgery for inguinal nodes). Patients with lymphadenopathy and an associated lymphocytosis should be referred directly to haematology. In patients with mild isolated lymphadenopathy and no concerning features, ultrasound may help assess nodal size and morphology and guide further management.

References

- NICE Clinical Knowledge Summary. Neck lump (May 2025) https://cks.nice.org.uk/neck-lump
- NICE Haematological cancers – recognition and referral (April 2025) https://cks.nice.org.uk/haematological-cancers-recognition-and-referral

Night sweats

Nights sweats are associated with lymphoma but night sweats as the sole presenting feature of lymphoma with no palpable lymphadenopathy, no weight loss and no blood count abnormalities would be unusual. The sweats should be drenching (e.g. need to change the bedclothes), usually occur at night and affect the whole body (not just one area e.g. back of neck).

Causes

- Infections – e.g. tuberculosis, endocarditis, osteomyelitis, abscesses, tropical infections
- Lymphoma
- Other malignancy e.g. lung cancer
- Neurological diseases e.g. autonomic dysfunction, Parkinson's
- Medications e.g. antidepressants, hormones e.g. tamoxifen – check BNF
- Withdrawal syndromes e.g. drugs, alcohol
- Endocrine issues
    - Hypoglycaemia
    - Phaeochromocytoma
    - Hyperthyroidism
    - Menopause
    - Carcinoid
- Autoimmune diseases
- Acid reflux
- Idiopathic

History and examination

Think about above causes and rule out systematically. Examine for lymphadenopathy and splenomegaly. Ask about travel.

Suggested investigations

- Full blood count and film
- Renal and liver function tests
- Inflammatory markers
- Calcium
- TSH
- Glucose or HBA1c
- Hormonal profile as appropriate
- HIV
- LDH
- Immunoglobulins and serum protein electrophoresis
- Chest radiograph
- Autoimmune screen if history suggestive

Management

This depends on the underlying cause. If there is associated weight loss or palpable lymphadenopathy then refer to haematology.

References

- NICE Haematological cancers – recognition and referral (April 2025) https://cks.nice.org.uk/haematological-cancers-recognition-and-referral

Raised ESR

The reference range depends on the patient's age and may be falsely elevated if the patient is anaemic or the sample has taken a long time to reach the laboratory. An ESR is non-specific and a CRP may be a better marker to screen for an infective/inflammatory disorder and is better for monitoring of most inflammatory disorders. Simultaneously checking a CRP and ESR is not advised.

Causes

- Infection
- Inflammation e.g. autoimmune disease, polymyalgia rheumatica
- Malignancy
- Increased immunoglobulins
- Myeloma or lymphoma
- Trauma
- Sarcoid

History and examination

Evaluate for any infective cause and look for any signs or symptoms of autoimmune disease. Ask about night sweats, bone pains and weight loss. Examine for lymphadenopathy and splenomegaly. Look at older blood results.

Suggested investigations

- Full blood count
- Blood film if cause unexplained
- Autoimmune screen if appropriate or suggestive
- Tests for infective aetiology
- Calcium
- Immunoglobulins and serum protein electrophoresis
- If no obvious cause consider chest radiograph and abdominal imaging

Management

This depends on the underlying cause and degree of suspicion. If there are no results or features to suggest haematological malignancy we do not review patients with an elevated ESR in haematology.

Iron deficiency

Ferritin <12 µg/L confirms absent iron stores, and <30 µg/L indicates iron deficiency. Ferritin 30 to 50 µg/L may still be consistent with iron deficiency, particularly in older adults and inflammatory states where ferritin can be elevated. A ferritin >50 µg/L usually excludes iron deficiency unless inflammation is present.

Low MCV and MCH support iron deficiency but are not sensitive; up to 50% of iron-deficient patients have a normal MCV. A normal FBC therefore does not exclude iron deficiency. If iron deficiency is suspected despite a normal ferritin, tests such as a blood film, reticulocyte haemoglobin or transferrin saturation may be helpful but we do not advise routine testing for 'iron studies'. Serum iron is not a good test for iron deficiency as it is affected by diet and diurnal variation and does not reflect iron stores.

Causes

- Blood loss
    - Blood donor
    - Gastrointestinal, gynaecological or urological blood losses
- Poor dietary intake of iron
- Malabsorption
- Increased requirements e.g. pregnancy, infancy, myeloproliferative neoplasms
- Paroxysmal nocturnal haemoglobinuria (extremely rare)

History and examination

Look for causes of blood loss. Quantitate menstrual blood loss. Ask about blood donation. Ask about malabsorption symptoms and diet. Enquire about travel history.

Suggested investigations

- Full blood count
- Coeliac screen
- *Helicobacter pylori*
- Stool parasite if relevant travel history and/or eosinophilia
- Urinalysis
- Ferritin (CRP if ferritin normal and suspect iron deficiency)
- If elevated inflammatory markers the following may be helpful: blood film, reticulocyte haemoglobin and transferrin saturation
- As directed by gastroenterology or gynaecology or urology e.g. endoscopies

Management

- We do not review patients with iron deficiency in haematology.
- Iron deficiency should be managed in primary care according to local and national guidance.
- Refer to the appropriate specialty for investigation of the underlying cause (e.g. gastroenterology, gynaecology or urology).
- Oral iron should be taken once daily, ideally in the morning on an empty stomach with vitamin C and away from acid-suppressing medication and foodstuffs containing tannins.
- Repeat the FBC after 4 weeks; haemoglobin should rise by approximately 20 g/L. Continue treatment for 3 months after anaemia resolves to replenish iron stores. aim ferritin over 50 µg/L
- Ongoing monitoring e.g. every three months and then annually for those at risk of further iron deficiency
- Continuous replacement may be required if ongoing losses e.g. heavy menstrual bleeding or malabsorption.

- Commercial "gentle iron" preparations may contain inadequate elemental iron for treatment of iron deficiency anaemia but may be considered as maintenance therapy
- Dietary changes are usually insufficient once patients are deficient in iron and supplementation is usually required
- For patients who do not tolerate oral iron, consider supportive care, an alternative preparation (e.g. with lower elemental iron), reduced or alternate-day dosing, liquid formulations, or taking treatment with food.
- If response to oral iron is inadequate, check adherence, optimise administration, and investigate for malabsorption (including coeliac disease and H. pylori) or other nutritional deficiencies.
- Patients should store iron supplements carefully to avoid accidental overdose

There is a specialist iron deficiency clinic at the RVI (run by gastroenterology) if further advice is required

Intravenous iron is generally only considered when patients are truly intolerant of oral supplements, after a trial of at least two different oral agents. There is some limited evidence that intravenous iron may work slightly quicker than oral iron and could be considered where a rapid rise in haemoglobin is required. In general, some indications for intravenous iron are below:

- Iron deficiency anaemia with intolerance of oral iron
- To support the use of erythropoiesis stimulating agents (including patients on renal dialysis).
- Persistent bleeding where taking oral iron is insufficient e.g. hereditary haemorrhagic telangiectasia
- Anaemia of chronic disease/inflammation where oral iron is poorly absorbed
- As an alternative to blood transfusion when a rapid increase in haemoglobin is required (e.g. perioperative anaemia, severe anaemia in late pregnancy or postpartum anaemia).

If intravenous iron is required urgently then this can be accessed via ambulatory care. In general speak to the relevant specialist or discuss with the iron deficiency service. We do not offer an IV iron infusion service in haematology.

References

- Snook J, Bhala N, Beales ILP *et al*. British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults. *Gut* 2021; **70**: 2030-2051. https://www.bsg.org.uk/clinical-resource/guidelines-iron-deficiency-anaemia-in-adults
- NICE Clinical Knowledge Summary. Anaemia – iron deficiency (July 2026). https://cks.nice.org.uk/topics/anaemia-iron-deficiency/
- Fletcher A, Forbes A, Svenson N, Thomas DW. Guideline for the laboratory diagnosis of iron deficiency in adults (excluding pregnancy) and children. *Br J Haematol* 2022; **196**: 523-529. https://b-s-h.org.uk/guidelines/guidelines/good-practice-paper-for-the-laboratory-diagnosis-of-iron-deficiency-in-adults-excluding-pregnancy-and-children
- Pavord S, Daru J, Prasannan N, *et al*. UK guidelines on the management of iron deficiency in pregnancy. *Br J Haematol* 2020; **188**: 819-830 https://b-s-h.org.uk/guidelines/guidelines/uk-guidelines-on-the-management-of-iron-deficiency-in-pregnancy/

Hyperferritinaemia

Ferritin is high if over 200 µg/L in women and over 300 µg/L in men.

Causes

- Any infection or inflammation including autoimmune conditions
- Liver disease and metabolic syndrome
- Malignancy
- Genetic haemochromatosis
- Renal failure
- Chronic blood transfusion
- Thalassaemia (even without blood transfusion)
- Myelodysplastic neoplasm
- Porphyria cutanea tarda
- Inherited anaemias including sideroblastic anaemia, congenital dyserythropoietic anaemia and some inherited haemolytic syndromes
- Hereditary hyperferritinaemia cataract syndrome
- Haemophagocytic lymphohistiocytosis
- Gaucher's disease
- Acaeruloplasminaemia

We do not see patients with high ferritin in haematology in Newcastle unless there is a suspected haematological cause such as thalassaemia, transfusion overload, other inherited anaemia or myelodysplastic neoplasm. This should be obvious from the history or blood count. We suggest following advice from the Newcastle genetics service: https://www.newcastle-hospitals.nhs.uk/services/clinical-genetics-service/information-for-healthcare-professionals/care-of-genetic-conditions-in-primary-care/hereditary-haemochromatosis/. The below references are also relevant.

If genetic haemochromatosis is suspected due to hyperferritinaemia and transferrin saturations above 40% in women or 50% in men then check *HFE* genotyping. This is available from primary care. If the patient is homozygous for *HFE* C282Y mutation or a compound heterozygote C282Y/H36D then suggest refer to Dr Steven Masson, consultant hepatologist. There are rare iron loading syndromes not due to mutations in the *HFE* gene and therefore if these are suspected (e.g. persistently elevated transferrin saturations above 40% in women or 50% in men or ferritin above 1000 µg/L and no secondary cause) then you may wish to discuss this with Dr Masson in the first instance.

References

- Cullis JO, Fitzsimons EJ, Griffiths WJ, Tsochatzis E, Thomas DW. Investigation and management of a raised serum ferritin. *Br J Haematol* 2018; **181**: 331-340. https://b-s-h.org.uk/guidelines/guidelines/investigation-and-management-of-a-raised-serum-ferritin/
- Fitzsimons EJ, Cullis JO, Thomas DW, Tsochatzis E, Griffiths WJ. Diagnosis and therapy of genetic haemochromatosis (review and 2017 update). *Br J Haematol* 2018; **181**: 293-303. https://b-s-h.org.uk/guidelines/guidelines/diagnosis-and-therapy-of-genetic-haemochromatosis-review-and-2017-update/

Vitamin B12 or folate deficiency

We do not see patients with vitamin B12 or folate deficiency. The cause of vitamin B12 or folate deficiency is usually dietary, due to malabsorption or autoimmune gastroenterological disorders.

We suggest following these two guidance documents:

- Vitamin B12 deficiency in over 16s: diagnosis and management. NICE guidance NG239 (March 2024) https://www.nice.org.uk/guidance/ng239
- Devalia V, Hamilton MS, Molloy AM. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *Br J Haematol* 2014; **166**: 496-513. https://b-s-h.org.uk/guidelines/guidelines/diagnosis-of-b12-and-folate-deficiency/

Elevated B12 levels

The reference range for serum B12 is 145-569 pmol/L. Elevated B12 levels can be seen in the normal healthy population.

Be aware that people of Black ethnicity may have a higher reference range for serum vitamin B12 concentrations than people of White or Asian ethnicity.

Causes

- Oral administration of supplements containing B12
- Ethnicity e.g. Black ethnicity
- Foodstuffs containing high levels of B12 e.g. energy drinks
- Liver disease
- Alcohol excess
- Renal disease
- Autoimmune disease
- Renal dysfunction
- Solid organ malignancy
- Haematological malignancy – especially myeloproliferative neoplasms and myeloma

History and examination

Ask about constitutional symptoms and alcohol intake. Look for signs of liver disease, autoimmune disease and splenomegaly. Any questions or examination that may point towards malignancy.

Suggested investigations

- Full blood count
- Renal and liver function
- If clinical concerns an autoimmune screen, blood film and immunoglobulins could be considered

Management

Elevated B12 levels are very non-specific. In the vast majority of cases a history, examination and check of full blood count and renal/liver function are all that is required. Dietary history including alcohol intake, supplements and energy drink consumption is important.

Further investigations should be tailored to the history and examination but in the absence of concerning symptoms or signs further invasive investigation is unlikely to yield positive results.

Prolonged clotting times and bruising

Coagulation tests are useful to screen for bleeding disorders in those with a suggestive bleeding history but alone are poorly predictive in assessing risk of bleeding pre-procedure. The ISTH bleeding assessment tool is a useful screening tool for bleeding history (ISTH-SSC Bleeding Assessment Tool Calculator). An abnormal coagulation screen does not necessarily increase the risk of bleeding and a normal coagulation screen does not necessarily rule out a bleeding disorder.

Indications for coagulation screens include:

- Before starting anticoagulation
- When investigating thrombocytopenia
- To look for a lupus anticoagulant
- Monitor anticoagulant (only request specific assay e.g. INR for warfarin)
- In the presence of a bleeding history
- Monitor severity of liver disease
- In patients with liver disease and high ASA grade pre-surgery

A common cause of a prolonged APTT is an interfering antibody, most commonly a lupus anticoagulant (LA). The laboratory will often perform additional tests automatically to determine the cause, with DRVVT being the confirmatory test for LA. LA is an antiphospholipid antibody and is often clinically insignificant, although it may be associated with antiphospholipid syndrome (APS) and other autoimmune diseases. Anticardiolipin and anti-beta-2 glycoprotein-1 antibodies may also be present in APS. Antiphospholipid antibodies occur in up to 5% of healthy individuals and may be transient. Repeat testing after 12 weeks may be appropriate if there are clinical features suggestive of APS, such as thrombosis, pregnancy morbidity, neurological symptoms or thrombocytopenia. In asymptomatic patients with an incidental LA, no further investigation is required.

Causes

Prolonged PT (or PT>APTT)	Prolonged APTT (or APTT>PT)	Prolonged PT and APTT	Bleeding disorders with normal coagulation
Warfarin	Lupus anticoagulant or other antibody interfering with assay	Disseminated intravascular coagulation	von Willebrand disease
Liver disease	Heparin	Anticoagulants	Platelet function defects
Vitamin K deficiency	Dabigatran	Coagulopathy due to trauma	Drugs e.g. antiplatelets, apixaban
Factor VII deficiency	Factor VIII, IX and XI deficiency	Major haemorrhage	Mild factor deficiency (including mild haemophilia)
Rivaroxaban/ apixaban	Factor XII deficiency (not a bleeding disorder)	Dysfibrinogenaemia	Factor XIII deficiency
	von Willebrand disease	High haematocrit	Connective tissue disorders e.g. Ehlers Danlos
	Dysfibrinogenaemia	Liver disease	Vitamin C deficiency
	High haematocrit (artefact)	Severe vitamin K deficiency	Uraemia
		Inherited deficiencies of factors II, V, X	Hereditary haemorrhagic telangiectasia

If the coagulation screen is unexpectedly abnormal suggest repeat in first instance as pre-analytical variables heavily affect results.

History and examination

Review previous results and exclude sampling from a line or anticoagulant effect. Assess for a personal or family history of bleeding, including excessive bleeding after surgery, dental procedures, trauma, menstruation, pregnancy, or spontaneous bleeding (e.g. epistaxis, gastrointestinal or intracranial haemorrhage).

The ISTH bleeding assessment tool is useful when taking a bleeding history (ISTH-SSC Bleeding Assessment Tool Calculator). If the score is over 3 in men or over 5 in women then please refer.

In patients with easy bruising, review medications and alcohol intake. In addition to anticoagulants, NSAIDs and antiplatelet agents, antidepressants may contribute to bruising. Vitamin C deficiency should be considered in malnourished patients. Bruising is common in older adults due to age-related skin changes and is also associated with long-term corticosteroid use. Examination should include assessment for lymphadenopathy, splenomegaly, signs of liver disease, hypermobility and hypothyroidism. A family history of a bleeding disorder should be sought. Consider non-accidental injury or abuse in cases of unexplained bruising. Please refer to the separate guideline on non-accidental injury.

Suggested investigations

- Full blood count and blood film (urgent)
- Repeat coagulation screen
- Renal and liver function
- TSH
- Urinalysis if a petechial rash
- Further investigations may have already been reflexed from the laboratory e.g. investigation for an antibody such as lupus anticoagulant or factor assays

Management

Management depends on the indication for testing and the results. If there is a personal or family history suggestive of a bleeding disorder, referral is recommended even if the coagulation screen is normal. Where an alternative cause of an abnormal coagulation result is identified (e.g. liver disease), discuss with the relevant specialty. If uncertain, seek advice via Advice and Guidance.

Sudden-onset bruising may be the first presentation of acute leukaemia. Features raising suspicion include weight loss, fever, hepatosplenomegaly, petechiae and pallor. If suspected, arrange an urgent full blood count and coagulation screen.

Easy bruising is common, particularly in older adults, and may be exacerbated by corticosteroids, antiplatelet agents or anticoagulants. If bruising is isolated, there are no other bleeding symptoms (particularly with previous uneventful surgery), the onset is recent, and the full blood count and coagulation screen are normal, an inherited bleeding disorder is unlikely.

References

- NICE Clinical Knowledge Summary. Bruising (March 2026). https://cks.nice.org.uk/topics/bruising/
- Lester W, Bent C, Alikhan R *et al*. A British Society for Haematology guideline on the assessment andmanagement of bleeding risk prior to invasive procedures. *Br J Haematol* 2024; **204**: 1697-1713. https://b-s-h.org.uk/guidelines/guidelines/the-assessment-and-management-of-bleeding-risk-prior-to-invasive-procedures
- ISTH Bleeding assessment tool: ISTH-SSC Bleeding Assessment Tool Calculator
- Biss T, Sibson K, Baker P *et al*. Haematological evaluation of bruising and bleeding in children undergoing child protection investigation for possible physical maltreatment: A British Society for Haematology Good Practice Paper. *Br J Haematol* 2022; **199**: 45-53. https://b-s-h.org.uk/guidelines/guidelines/haematological-evaluation-of-bruising-and-bleeding-in-children-undergoing-child-protection-investigation-for-possible-physical-maltreatment

Thrombophilia

A "thrombophilia screen" is a test for a variety of factors predisposing to venous thrombosis. With the exception of lupus anticoagulant (see above), the results are irrelevant for the management of arterial thrombosis. For patients with unexplained arterial thrombosis different tests may be appropriate and should be discussed with the appropriate specialist (e.g. stroke physician, cardiologist, vascular surgeon).

There are surprisingly few indications for inherited thrombophilia testing and it is not usually appropriate outside of specialist thrombosis clinics. This is because:

1) The test is not exhaustive so a negative test does not rule out an inherited tendency to thrombosis.
2) Most people who carry the most common prothrombotic abnormalities e.g. factor V Leiden will never have a thrombosis, so a positive result should not influence management. Screening asymptomatic family members is therefore not advised.
3) Patients with a provoked thrombosis would usually have a time-limited period of anticoagulation and stop regardless of a thrombophilia screen result.
4) Patient with unprovoked thrombosis are often offered on going anticoagulation, regardless of a thrombophilia screen result.
5) A family history of venous thrombosis in a first degree relative is a relative contraindication to the use of oestrogen-containing contraceptives and oral oestrogen-containing HRT (transdermal HRT used at standard doses is not thought to increase the risk of VTE) irrespective of the presence or absence of a defined thrombophilia. Family screening for inherited thrombophilia in asymptomatic patients is not advised.
6) Diagnosing inherited conditions may impact on other aspects of life e.g. insurance

A demand management process is in place to screen requests and contact numbers for the consultant haematologists involved in this provided to allow requestors to discuss processing of individual samples.

We would encourage all requests for inherited thrombophilia to be discussed with a haematologist.

When deciding on whether to perform a thrombophilia screen we generally follow this guideline from the British Society for Haematology: Arachchillage DJ, Mackillop L, Chandratheva A, Motawani J, MacCallum P, Laffan M. Thrombophilia testing: A British Society for Haematology guideline. *Br J Haematol* 2022; **198**: 443-458. https://b-s-h.org.uk/guidelines/guidelines/guidelines-for-thrombophilia-testing

Venous thromboembolism and travelling

Venous thromboembolism occurs in travellers due to immobility, direct compression of the venous system at the back of the knee and possible activation of the coagulation system in response to air travel. However, the absolute risk of VTE in travellers is low. The absolute risk of VTE in healthy people has been calculated as one event per 106 667 flights for flights lasting less than four hours, and one event per 4656 flights, for flights lasting over four hours. Risk increases with the duration of flight. There is little evidence with which to make firm recommendations.

Risk factors for VTE include:

- Previous DVT or PE off anticoagulants
- Active malignancy
- Recent surgery or trauma, particularly to the abdomen, pelvis, or legs in last four weeks
- A family history of VTE in first degree relative
- Aged over 60 years
- Inherited thrombophilia
- Large varicose veins or chronic venous insufficiency
- Limited mobility (for example, a lower-limb fracture in plaster)
- Obesity (body mass index greater than 30 kg/m^2)
- Myeloproliferative neoplasms
- Pregnancy, or up to six weeks postpartum
- Prothrombotic state e.g. autoimmune or inflammatory conditions
- Use of oestrogens, such as oral contraceptives or hormone replacement therapy.

Management

Counsel patients with higher risk of VTE and allow them to make a decision as to whether flights should be postponed until the risk reduces.

In patients with a personal history of VTE we take the pragmatic solution of offering either a prophylactic dose of LMWH or rivaroxaban in all flights over four hours. If their thrombotic event was associated with a flight less than four hours we offer this for all flights. There is little good quality evidence for which to advise on other scenarios but if there are multiple risk factors then a similar regime can be considered. Rivaroxaban has the advantage of not requiring any sharps bins. We advise to take one 10 mg dose prior to flying (each way) for every 24 hours in flight. For example a six hour flight would need one 10 mg dose outbound and one dose for the return but if a fight or journey lasted more than 24 hours then a second dose would be required each way. If LMWH is used, use a pre-filled syringe and ensure patients are able to administer. Provide written information on the need for needles and provide a sharps bin.

For patients with other risk factors class 1 stockings (exerting a pressure of 14–17 mmHg at the ankle) or proprietary flight socks can be considered. These are contraindicated if the ABPI is less than 0.8. Aspirin is not advised. Patients should move around frequently and perform calf compression exercises. Keeping hydrated seems sensible but there is no evidence to suggest it reduces risk of VTE. Patients should inform their travel insurance company of any pre-existing medical problems. It is sensible to offer advice on the signs and symptoms of VTE in those at risk and the need to present if these develop.

References

- NICE Clinical Knowledge Summary. DVT prevention for travellers (November 2023). https://cks.nice.org.uk/topics/dvt-prevention-for-travellers/

Superficial thrombophlebitis

Please see separate guideline on this.

Haemoglobinopathy and thalassaemia

Haemoglobinopathies comprise:

1. Thalassaemias (reduced production of alpha or beta globin chains).
2. Haemoglobin variants (structural abnormalities of haemoglobin, e.g. sickle haemoglobin).

These conditions occur in all ethnic groups but are more common in people with African, Caribbean, Middle Eastern, Mediterranean, South Asian and South-East Asian ancestry.

Referral Guidance

Refer to Haematology

Urgent

- Sickle cell disease (new diagnosis or patient moving into the area)
- Transfusion-dependent thalassaemia
- Transfusion-dependent rare anaemia

Routine

- HbH disease (three-gene alpha thalassaemia)
- Rare inherited anaemia patients who are not transfusion dependent (e.g. pyruvate kinase deficiency, congenital dyserythropoietic anaemia, Diamond Blackfan anaemia)
- Other clinically significant haemoglobinopathies

Refer to clinical genetics

Couples found through haemoglobinopathy screening to be at risk of having a child with a clinically significant haemoglobin disorder should be offered genetic counselling and consideration of reproductive options, including pre-implantation genetic testing where appropriate, through clinical genetics.

Seek Advice & Guidance from haematology

- Uncertain interpretation of haemoglobinopathy results
- Suspected alpha thalassaemia where diagnosis is unclear
- Significant anaemia or erythrocytosis with an abnormal haemoglobinopathy screen
- Both partners are carriers of a haemoglobinopathy and/or thalassaemia

Conditions that usually do not require haematology referral

- Beta thalassaemia trait
- Likely alpha thalassaemia trait
- Sickle cell trait
- Isolated haemoglobin variant carrier states (e.g. HbC trait, HbE trait)

Patients planning pregnancy who have a known haemoglobin variant or thalassaemia trait should be advised that their partner undergoes a full blood count and haemoglobinopathy screen.

Investigation in primary care

When to request a haemoglobinopathy screen

- Persistent unexplained microcytosis (especially with normal or raised RBC count)
- Blood film suggestive of a haemoglobinopathy/thalassaemia
- Family history of a haemoglobinopathy/thalassaemia
- Partner known to carry a haemoglobinopathy/thalassaemia

When requesting advice, please include:

- Serum ferritin
- Ethnicity/family origin
- Relevant clinical history

Thalassaemia

Thalassaemia trait is a carrier state rather than an illness and is commonly identified during investigation of microcytosis.

Features suggestive of thalassaemia trait (alpha or beta)

- Persistently low MCV
- Normal or raised RBC count
- Mild or no anaemia

This pattern differs from iron deficiency, where RBC count is often reduced.

Do not use MCV as a marker of iron status in patients with known or suspected thalassaemia. Iron deficiency should be assessed using serum ferritin. Patients with thalassaemia trait may have mild anaemia, but haemoglobin is usually above 100 g/L. New or worsening anaemia should be investigated using standard anaemia pathways.

Beta thalassaemia trait

In beta thalassaemia trait there is an elevated HbA_2 on haemoglobinopathy screening. It is a benign carrier state and does not require haematology referral. Patients planning pregnancy should be advised that their partner has a full blood count and haemoglobinopathy screen.

Alpha thalassaemia trait

Alpha thalassaemia trait is more common than beta thalassaemia trait and is not detected by routine haemoglobinopathy screening. Diagnosis is usually based on red cell indices as above and normal serum ferritin. Most individuals are asymptomatic and require no treatment. Where both partners may carry alpha thalassaemia, seek Advice & Guidance due to reproductive implications.

Sickle cell diseases and haemoglobin variants

Clinically significant sickle syndromes include:

- HbSS – homozygous sickle cell anaemia
- Other significant compound heterozygous haemoglobinopathies e.g HbSC, HbS/β-thalassaemia

All patients with sickle cell disease should be referred to haematology.

Common haemoglobin variants include:

- HbS
- HbC
- HbD
- HbE
- Hb O-Arab
- Hb Lepore

Individuals carrying a single variant are usually asymptomatic and generally do not require referral.

Screening and counselling

Newborn screening

In the UK, newborn screening includes testing for sickle cell disease. Thalassaemia is not always diagnosed through newborn screening.

Antenatal screening

Pregnant women are offered screening for haemoglobinopathies. Significant haemoglobin disorders may occasionally be identified for the first time during pregnancy.

Reproductive counselling

Most carrier states have little or no clinical impact on the individual but may have important implications for offspring. Partner testing should be arranged when:

- Beta thalassaemia trait is identified

- Alpha thalassaemia trait is suspected
- A clinically significant haemoglobin variant is identified

Seek Advice & Guidance or refer to Clinical Genetics if both partners carry clinically significant haemoglobinopathy traits and/or are carriers for thalassaemia.

Key messages for primary care

- Persistent microcytosis with a raised RBC count strongly suggests thalassaemia trait.
- Alpha thalassaemia is not detected by routine haemoglobinopathy screening.
- Use serum ferritin rather than MCV to assess iron deficiency.
- Most carrier states require no treatment and do not require haematology referral.
- Refer all patients with clinically significant sickle cell disease or transfusion-dependent thalassaemia.
- Consider the reproductive implications of all haemoglobinopathy carrier states and arrange partner testing where appropriate.

Blood parasite investigation

A number of parasites can be detected by blood film microscopy including malaria, microfilaria, trypanosomes and babesia. Timing of sample and clinical details is critical for accurate interpretation.

Malaria
There are five recognised species of malaria parasites affecting humans: *Plasmodium falciparum*, *P vivax*, *P ovale*, *P malariae* and *P knowlesi*. Patients can present with fever, myalgia, headache, nausea, diarrhoea, vomiting, lethargy, anorexia and rigors. Rarely symptoms of malaria can manifest many years after exposure.

In patients returning from a malarial endemic region presenting with symptoms concerning for malaria the following initial investigations are suggested

- Full blood count
- Thick and thin blood films (the laboratory will automatically calculate level of parasites in cases of *P falciparum* and *P knowlesi*)
- Malaria rapid diagnostic test (this will be done automatically by the laboratory)
- Renal and liver function
- CRP

It is vital that details of anti-malarial medication and travel history are given with each request. When investigation for malarial parasites is requested the sample should be transported to the laboratory as soon as possible. A negative malarial screen does not exclude a diagnosis of malaria. If there is strong clinical suspicion of malaria repeat the test in 12, 24 and 48 hours. If concerns please discuss with an infectious diseases specialist registrar or consultant.

Microfilaria
Filariasis in humans can give rise to a variety of clinical features; these include eosinophilia, chyluria, elephantiasis, lymphadenopathy, Calabar swelling, urticaria, subcutaneous nodules and blindness.

In patients returning from an endemic region presenting with symptoms concerning for microfilaria the following initial investigations are suggested

- Full blood count
- Thick and thin blood films
- Filaria serology

The timing of specimen sampling is critical in the detection of microfilaria. Times for collection should be selected in accordance with the patient's clinical symptoms and travel history. An absolute minimum of a sample taken during the day (around 1pm) and one at night (around midnight) should be examined. It is vital that details of travel history are given with each request. If concerns please discuss with an infectious diseases specialist registrar or consultant as normal blood film microscopy does not exclude this diagnosis.

Trypanosomes
Patients infected with trypanosomes can present with fever, headaches, joint pains, itching and lymphadenopathy. The symptoms can vary depending on the type of trypanosome.

In patients returning from an endemic region presenting with symptoms concerning for trypanosome infection the following initial investigations are suggested

- Full blood count
- Thick and thin blood films

- Trypanosome serology

If concerns please discuss with an infectious diseases specialist registrar or consultant as normal blood film microscopy does not exclude this diagnosis.

Babesiosis
Babesiosis occurs following tick bites; particularly in immunocompromised patients and patients who have hyposplenism. Babesia infection is characterised by the presence of haemolytic anemia and nonspecific flu-like symptoms (e.g. fever, chills, myalgia, weakness, fatigue). Some patients have splenomegaly, hepatomegaly, or jaundice. Risk factors for severe babesiosis include asplenia, advanced age and other causes of impaired immune function (e.g. HIV, malignancy, corticosteroid therapy, chemotherapy).

In patients returning from an endemic region presenting with symptoms concerning for babesiosis the following initial investigations are suggested:

- Full blood count
- Thick and thin blood films

It is vital that details of travel history are given with each request. If concerns please discuss with an infectious diseases specialist registrar or consultant as normal blood film microscopy does not exclude this diagnosis.