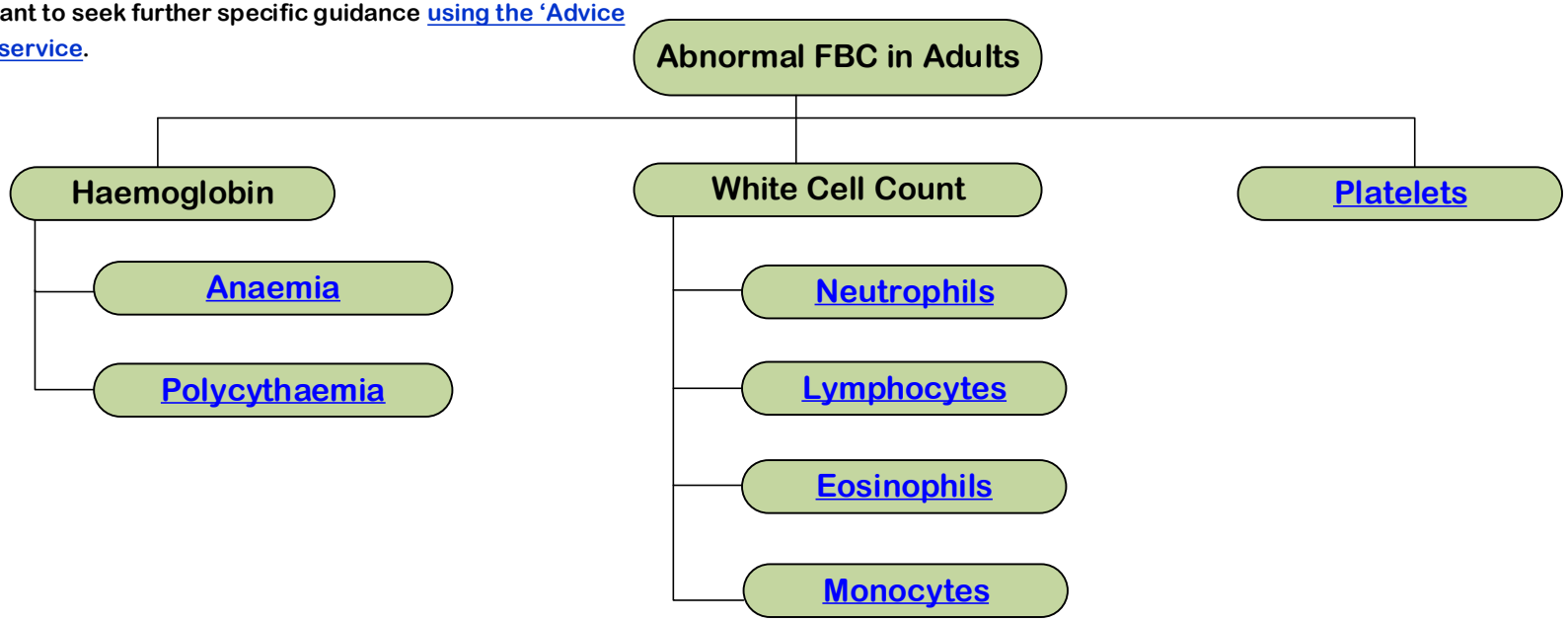
Abnormal FBC Results Guidance

Please refer to the Summary of Product Characteristics (SPC) of any drug considered.

This pathway has been developed from published guidance in collaboration with local haematologists and gastroenterologists.

This guidance is to assist GPs in decision making and is not intended to replace clinical judgement.

You may also want to seek further specific guidance using the 'Advice and Guidance' service.



NB – Abnormalities affecting more than one cell type are more likely to be due to bone marrow causes rather than reactive. Always consider earlier referral when the patient is unwell.

Produced in collaboration with local Haematologists and Gastroenterology
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Consider mixed deficiency and look at the whole picture

Anaemia
Hb < 130g/L Men (over 15 yrs of age)
Hb < 120g/L Non-pregnant women (over 15 yrs of age)

Monitor FBC for evidence of progression over time

Mean Corpuscular Volume (MCV)

MCV <95fl

Check ferritin
(Note: Ferritin can be raised in the presence of inflammation, infection, malignant disease or liver disease)

Low ferritin
<15 micrograms/L

Iron deficiency anaemia
(Camden iron deficiency pathway)

Indeterminate
ferritin 31-99 micrograms/L
with no known inflammatory states

Iron studies including serum iron/ TIBC/ iron saturation

CRP> 30mg/L
Iron <7 micromol/L
Iron saturation <20%
TIBC <45 micromol/L

Functional iron deficiency
Refer to iron deficiency pathway and refer to appropriate specialist where anaemia of chronic disease is suspected

CRP normal/elevated
Iron> 7micromol/L
Iron saturation >20%
TIBC >45 micromol/L

Iron replete

High ferritin
>100 micrograms/L

Non-iron deficient microcytic anaemia or functional iron deficiency
Consider:
Non-haemotological Cause
- Acute/ chronic inflammation
- Chronic infection
- Malignancy
- Liver disease (see abnormal liver function pathway)
- Renal failure
- Anaemia of chronic disease

Haemotological Cause:
- Haemoglobinopathy (eg; thalassaemia trait)
  Screen if no previous Hb electrophoresis result
- Sideroblastic anaemia

Refer to appropriate specialty as necessary.

MCV >95fl

Review history, duration, symptoms, bleeding, diet, medication, alcohol, family history, recent transfusion

Check LFTs (including GGT), B12, folate, TFTs and renal function

Check reticulocyte count and blood film

Reticulocyte count <80x10^9/L

Reticulocyte count >80x10^9/L

Check serum folate
And serum B12

Serum B12

<200ng/L

Symptomatic

Commence B12 replacement
(see table)

For people with neurological involvement seek urgent specialist advice from haematologist

Non-symptomatic

Recheck B12 in 2 months
If B12>200ng/L no further investigation.
If B12 still <200ng/L refer to gastroenterology for IF antibody

>200ng/L but strong clinical suspicion of B12 deficiency*

Check intrinsic factor (IF) antibody

Serum folate

<3 micrograms/L

3 - 4.5 micrograms/L and symptomatic

Ensure B12 normal.
Folate replacement see table & monitor response

If serum folate and B12 normal and patient not symptomatic investigate for:
- Liver disease
- Alcohol misuse
- Hypothyroidism
- Drug causes
- Haemotological disorder

If myelodysplasia or myeloma suspected or if cause of anaemia unknown refer to a haemotologist

Possible haemolysis

Check bilirubin

Normal bilirubin

Possible bleed
Investigate as indicated by history

Raised bilirubin

Blood film, LDH, direct anti-globulin test

Refer to haemotology

*False normal B12 assays can lead to undetected vitamin B12 deficiency. When B12 deficiency is suspected on the basis of clinical findings, check IF

Urgently refer to haematology
- Leycoerythroblastic anaemia on blood film
- Unexplained progressive symptomatic anaemia
- Associated splenomegaly lymphodenopathy and other cytopenias
- Suspected haemotological malignancy or other blood disorders (2WW)

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Treatment for Vitamin B12, folate or Iron deficiency

Vitamin B12 replacement

Give dietary advice to all patients.

For people with neurological involvement
Seek urgent advice from haemotologist
If advice not immediately available consider following whilst waiting:
Hydroxocobalamin 1mg IM on alternate days until there is no further improvement, then administer hydroxocobalamin 1mg IM every 2 months

For people without neurological involvement
Hydroxocobalamin 1mg IM three times a week for 2 weeks. Thereafter give maintenance therapy dependent on cause of deficiency.

Non dietary cause: Hydroxocobalamin 1mg IM 3 monthly
Dietary cause: Hydroxocobalamin 1mg IM 6 monthly or
Oral cyanocobalamin tablets 50-150 micrograms daily in those unwilling to take injectable therapy.
Hydroxocobalamin is the form of vitamin B12 of choice as it is retained in the body longer than cyanocobalamin.

Folate replacement

- Prescribe oral folic acid 5mg daily usually for 4 months. If underlying cause of deficiency is persistent, supplementation may need to be taken for longer (sometimes for life)
- Check vitamin B12 level in all people before starting folic acid- treatment can improve wellbeing, mask underlying B12 deficiency and allow neurological disease to develop
- Give dietary advice

Iron replacement

See iron deficiency pathway (Camden Iron Deficiency Pathway)

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Polycythaemia / erythrocytosis

Men: Hb > 185 g/L Hct > 0.52
Women: Hb > 165 g/L Hct > 0.48

FBC should be repeated after a minimum of one week to determine if rise is transient. Previous results should also be rechecked to determine whether the trend was previously present.
NOTE: Hct is a better marker in identifying patients with a raised red cell mass than haemoglobin concentration.

May be associated with increased WCC & Platelets
NOTE: Smokers have a significantly higher neutrophil count than non-smokers.
Neutrophilia is defined as >12·5 × 10⁹/l in smokers.

Probable 1° erythrocytosis (Ferritin usually low)

Causes of Polycythaemia
Polycythaemia leads to increased blood viscosity, and elevated risk of thrombosis. For all people with polycythemia/erythrocytosis, manage cardiovascular disease risk factors, including hyperlipidaemia, diabetes, hypertension, and smoking.

Apparent erythrocytosis
Caused by reduced plasma volume
Common in obese men, associated with smoking, diuretics, alcohol, hypertension, stress, dehydration
At risk of occlusive vascular episodes

Address factors that may reduce plasma volume and repeat blood sampling in two months. If Hct has not normalised, further tests may be required to rule out secondary erythrocytosis/ polycythaemia vera.
People with confirmed apparent erythrocytosis should be offered a blood test every 3-6 months and if HCT > 0.45 on two consecutive occasions, refer to haematology.

Absolute erythrocytosis
1° erythrocytosis caused by polycythaemia vera (92% are JAK2 +ve)

2° erythrocytosis caused by:
Hypoxia
(COPD,Heart disease, smoking)
Abnormal EPO production
(Renal & liver tumours, fibroids)

Consider checking LFTs, urea and electrolytes and eGFR to rule out differential diagnoses.

WCC & Platelets normal

Probable 2° erythrocytosis (ferritin usually normal)

Refer to an appropriate specialist to ensure optimal management of underlying cause.
Patients with a risk factors for apparent erythrocytosis, or signs and symptoms suggestive of 2° erythrocytosis, and without signs or symptoms suggestive of polycythaemia vera should be retested in two months following attempts to address apparent / 2° erythrocytosis. Repeat abnormal results should prompt a referral

Refer
The following groups of patients should also be referred:

- Raised Hct >0.52 males + Past history of arterial or venous thrombosis
  >0.48 females splenomegaly, pruritus, elevated WCC or platelets
  (uncuffed blood samples)
- Or if persistent, unexplained raised Hct above these levels on at least 2 occasions over 2-4 weeks apart.

Urgently Refer: (2wks)
Hb >200 g/l / Hct > 0.60 (in absence of chronic hypoxia)

Raised Hb in association with:
Recent arterial or venous thrombosis
Neurological Symptoms
Visual Loss
Abnormal bleeding

If polycythaemia vera is suspected and/or the person is experiencing symptoms of hyperviscosity refer urgently to haematologist

Eosinophilia

> 0.5 x 10⁹/L

Check history:
Drugs, Travel, Atopy
Check history of skin rashes or lymphadenopathy. Cardiorespiratory and gastrointestinal symptoms should be evaluated.
Constitutional symptoms should be noted including fever, drenching night sweats, weight loss, pruritus and alcohol-induced pain.
Repeat FBC + Blood Film within 1-2wks

Mild to moderate eosinophilia (0.5 – 1.5 x10⁹/ L) in patients who are otherwise well may not require further investigation

Patients with systemic symptoms and those with persistent eosinophilia (≥ 1·5 × 10 ⁹ /l), irrespective of suspected organ damage

Consider the following investigations dependent on the suspected cause.

In those with a suspected infectious cause:
- Fresh stool microscopy for ova, cysts and parasites
- Serological tests for suspected parasitic infections e.g. strongyloidiasis, schistosomiasis, filariasis, toxocariasis where appropriate

In those with a suspected connective tissue disorder:
- Antinuclear activity (ANA)

In those with a suspected vasculitis:
- Antineutrophil cytoplasmic antibodies (ANCA)

In those with suspected respiratory disease:
- Appropriate imaging e.g chest x-ray

Discuss with microbiology / ID as appropriate

Eosinophils >1.5 persisting >3mths or rising without obvious cause

Refer to haematology

Eosinophilia causes to consider:

- Asthma / allergic disorders
- GI disorders (e.g. chronic pancreatitis, inflammatory bowel disease, coeliac disease, primary GI eosinophilic disorders including eosinophilic oesophagitis)
- Infections (esp. Parasitic eg. Schisto, also malaria, TB, fungal, recovery from any infection)
- Drugs (eg. penicillin, allopurinol, amitriptylline, carbamazepine)
- Smoking
- Connective tissue disorders (eg. Rheumatoid arthritis, polyarteritis nodosa, Churg-Strauss, Systemic lupus erythematosus, eosinophilic fascitis (shulman disease))
- Endocrine (eg. Addison's)
- Skin disease (Eczema, psoriasis, dermatitis herpetiformis, erythema multiforme)
- Malignancy (eg. Lymphoma, Leukaemia, solid tumours)
- Löffler's syndrome, Endocarditis, Post-splenectomy, Irradiation

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Lymphocytes

Normal 1.3 – 3.5 x10⁹/L (20-45%)

Low — Raised

If features of viral illness & otherwise well, Repeat test in 4-6 weeks once symptoms resolved

Lymphopenia

Causes of Lymphopenia

- Drugs (eg. steroids)
- Infection – postviral common (exclude HIV, legionella)
- Malignancy (marrow infiltration, post chemo/ radiotherapy, **myeloma – consider v urgent protein electrophoresis and BJP if suggestive symptoms**)
- Renal or hepatic impairment
- Connective tissue (eg. RA, SLE, sarcoid)
- Anorexia Nervosa
- Primary immune deficiency

Refer for treatment of underlying cause

Note: Lymphopenia in many cases is transient and may not require specialist input. If lymphocyte count remains low on repeat testing refer

Monocytosis
Monocyte count
> 0.8 x 10⁹/L

Raised in malaria, typhoid, TB, MDS, CMML(persistently >1.5)

Repeat and Refer if persists

Lymphocytosis

If > 20 x 10⁹/L *or* Lymphadenopathy, Splenomegaly, Anaemia, other cytopenia, weight loss, night sweats, PUO

Refer urgently

If no red flag symptoms check IM screen and repeat 4 – 6 weeks

Refer to haematologist If persisting

Causes of Lymphocytosis

- Infection eg EBV, CMV, Pertussis, Mumps, Rubella
- Stress
- Vigorous exercise
- Post splenectomy
- Haem Malignancies eg ALL, CLL, NHL

Neutrophils

Normal 2.0 – 7.5 x10⁹/L 40 - 75 %

Low — Raised

Neutropenia

(Isolated neutropenia is v.common)

<1.0 x 10⁹/L

Unwell, febrile or on chemotherapy, lymphadenopathy, splenomegaly, other cytopenia

Emergency Referral

Well and afebrile- Check blood film. If blood film normal: Repeat FBC & blood film in 1 week

Refer urgently if persists

1–1.5 x 10⁹/L

Check blood film +/- B12, folate, ferritin, ANA

Repeat FBC 4 – 6 wks

Refer if persists and unexplained or if other fbc abnormalities or if history of recurrent infections/ ulcers

Causes of Neutropenia

- Infection (EBV, Hep B,C, HIV)
- Ethnic variation: common in Afro-Caribbean, SE Asian
- Drugs (eg. phenytoin, carbimazole, antipsychotics, clotrimoxazole)
- Endocrine (eg. thyroid)
- Malignancy (marrow infiltration, chemo/radiotherapy, **myeloma – consider v urgent serum electro and urine BJP if suggestive symptoms**)
- Connective tissue disorder (eg. RA, gout)
- Autoimmune
- B12, folate, iron deficiency
- Excess alcohol
- Liver disease (cirrhosis)

Neutrophilia

>7.5 x 10⁹/L

Infection most common cause

Repeat FBC 4-6wks with inflammatory markers

Refer if Cause unclear, unable to manage in primary care, persistant neutrophilia

Refer if > 15 x 10⁹/L Or associated splenomegaly Or other FBC abnormalities

Causes of Neutrophilia

- Infection (Bacterial, some viral eg VZV,HSV, some fungal & parasitic)
- Drugs (eg. steroids)
- Malignancy (eg.Carcinoma,LymphomaLeukaemia)
- Connective tissue disorder (eg. RA, gout)
- Haemorrhage, haemolysis, hypoxia, tissue damage, infarction

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Check history: travel, drugs, alcohol

Ask about bleeding history:
Spontaneous skin/mucosal bleeding, bruising, GI bleeding, epistaxis, gums, menorrhagia.
Post dental / surgical haemorrhage
Haemarthoses / muscle haematomas

Platelets

Normal 150 - 400 x10⁹/L

Thrombocytopenia

Often artefact
Repeat with blood film

< 150

< 50 x10⁹/L

Urgent Referral

If < 20 x10⁹/L or any bleeding
Refer for same day assessment

50-100 x10⁹/L

If no red flag symptoms and unexplained thrombocytopenia persists > 4-6 weeks - Refer

If other cytopenia, splenomegaly, lymphadenopathy, pregnancy, upcoming surgery
Urgent Referral

100-150 x10⁹/L

Repeat monthly & Refer if progressive decrease, other FBC abnormalities or if unwell

Thrombocytopenia

Viral infection including EBV
(usually resolves within few weeks)
Also HIV, Malaria, TB

Drugs
(NSAIDs, Heparin, Digoxin, Quinine, anti-epileptics, antipsychotics, PPIs)
Alcohol

Malignancy
Liver & Renal disease

Aplastic anaemias,
B12/Folate deficiency
Autoimmune / ITP / SLE

Thrombocytosis

> 400

Urgently Refer:
- Abnormal bleeding
- Neurological symptoms
- Plt > 1000 x10⁹/L *or*
- > 600 x10⁹/L with recent thrombosis or at high risk thromboembolism or CVD
- Splenomegaly
- Other symptoms suggestive malignancy
- Other significantly abnormal FBC indices

Check for hepato/splenomegaly or neuro symptoms

Check CRP, blood film, ferritin

If asymptomatic repeat FBC after 4-6 wks

< 450 x10⁹/L

No further action required

>450 x10⁹/L

Treat 2° causes

Check Hb / ferritin (Polycythaemia?)

Refer to haematology if persistent unexplained thrombocytosis
> 600 x10⁹/L
on at least 2 occasions
4-6 weeks apart

Or 450-600 x10⁹/L
in association with other FBC abnormalities

Thrombocytosis

1° - Myeloproliferative (likely if splenomegaly and plt >1000)
2° - More common:
- Reactive (Infection, inflammation, haemorrhage, exercise, tissue damage, post surgery, haemolysis)
- Malignancy
- Hyposplenism/ Splenectomy
- Iron deficiency