Contents

1. Lymphadenopathy
2. Splenomegaly
3. Lymphocytosis
4. Lymphopenia
5. Neutropenia
6. Neutrophilia
7. Eosinophilia
8. Polycythaemia
9. Thrombocytosis
10. Thrombocytopenia
11. Paraprotein
12. Microcytic anaemia
13. Normocytic or Macrocytic Anaemia
14. Macrocytosis
15. Pancytopenia
16. Hyperferritinaemia
**Lymphadenopathy**

B Symptoms
- Weight loss >10% over 6 months
- Drenching sweats,
- Unexplained fever >38°C

Lymphadenopathy associated with:
- B symptoms
- Liver and spleen enlargement
- Rapidly increasing in size
- Generalised lymphadenopathy
- Cytopenias

Refer to Haematology on urgent (suspected cancer) pathway

Localised unexplained adenopathy
OR
Concerns of metastatic node

Appropriate referral to surgical team or ENT for biopsy/ radiological biopsy (US or CT guidance)

**Causes:**
- Acute and chronic bacterial infections
- Syphilis
- Auto immune conditions
- Malignancy (haematological/ metastatic)
- Viral infections (including HIV, EBV, CMV)
Splenomegaly

**B symptoms**
- weight loss >10% over 6 months
- drenching sweats,
- unexplained fever >38°C

**NB:** Spleen increases with height. On average increases in length by 0.2 cm for every inch > 6 ft

**Spleen >13 cm**

**If Criteria not met for urgent referral look for causes**

- **B symptoms**
- Cytopenias
- Increased LDH
- Paraprotein
- Lymphadenopathy
- high haemoglobin or increased platelet count
- Evidence of haemolysis
- High WBC
- Leuco-erythroblastic blood film

**Refer to Haematology on urgent (suspected cancer) pathway**

**Causes**
- Infections – Viral (HIV, EBV, CMV) and parasitic
- Alcohol
- Liver disease
- Cardiac failure
- Autoimmune
- Lymphoproliferative disorders
- Myeloproliferative disorders (such as CML or myeloproliferative disorders)
- Haemolysis

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Lymphocytosis

8 Symptoms
- Weight loss >10% over 6 months
- Drenching sweats,
- Unexplained fever >38°C

• Lymphocytosis >20x 10^9/L
• Other cytopenias
• B symptoms
• Lymphadenopathy
• Splenomegaly

Refer urgently (suspected cancer) to haematology

Lymphocytosis >5x 10^9/L

• Lymphocytosis 5-20x 10^9/L
• Repeat FBC in 6 weeks and look for causes

Lymphocytosis 5-20x 10^9/L

- If <10x 10^9/L monitor 6 monthly
- If persistent >10x 10^9/L refer routinely to Haematology

Causes:
- Smoking
- Viral infections especially Glandular fever
- Lymphoproliferative disorders (such as CLL)
- Bacterial infections
- Post-splenectomy
- Rheumatoid arthritis

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**Lymphopenia**

**Red Flag signs**
- Weight loss
- Fevers
- Drenching night sweats
- Recurrent infections

**Causes:**
- Elderly patients
- Infections including HIV, hepatitis B and C
- Excess alcohol
- Malnutrition
- Medications-steroids, chemotherapy
- Systemic immune conditions
- Systemic illness(renal, cardiac, liver failure, malignancy)
- Lymphoma

**Pathway for Lymphopenia**

If lymphocytes <1.0x10^9/L

- If lymphocytes <1 and red flag symptoms
  - Lymphocytes <1 and red flag symptoms

- If >0.5x10^9/L and >70 years of age no need for further investigations

- If no red flag symptoms repeat FBC in 6 weeks and look for causes

If no obvious cause and persistent over 6 months refer routinely to Haematology

If lymphocytes <1 and red flag symptoms

- Lymphocytes <1 and red flag symptoms

**Patient Information**
- TBC

**Referral Proforma**
- TBC

**Local Guidance**
- TBC

**National Guidance**
- TBC

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Neutropenia

Causes To Consider
- Drugs
- Myeloma
- B12/folate deficiency
- Autoimmune
- Any viral infection including HIV/Hepatitis B/C

Neutrophil Count <1.8 x 10^9/L

- Neutrophil Count <0.5 x 10^9/L
  - Patient well with no fever
  - Evidence of sepsis
    - If no obvious cause (see box above) refer urgently (suspected cancer) to Haematology
    - Admit to hospital for management of Neutropenic sepsis

- Neutrophil Count 0.5 - 1 x 10^9/L
  - Repeat FBC in 1 week and look for causes

- Neutrophil Count >1 x 10^9/L
  - Repeat FBC in 6 weeks and look for causes
  - If persistently <1.0 x 10^9/L and no obvious cause found, refer to Haematology
  - If between 1.0-1.8x 10^9/L then monitor annually.

Note:
- A neutrophil count of between 1-5 - 2.0 x 10^9/l whilst below the normal range is unlikely to be of any clinical significance.
- People of Afro-Caribbean or Middle Eastern ethnicity have a lower normal range for the neutrophil count (constitutional or ethnic neutropenia) 1 - 1.8 x 10^9/l. This is of no clinical consequence. Only refer if their neutrophils are <1.0 x 10^9/l on repeat testing.
Neutrophilia

Neutrophil count elevated
If chronic myeloid leukaemia is suspected you will be contacted by a haematologist to organise urgent admission or outpatient review and further investigations as indicated

Assess if there is a clear cause for this:
• Infection
• Inflammation
• Steroids
• Pregnancy
• Smoking
• Underlying neoplasia

If cause unclear check:
• Blood Film
• ESR
• CRP
• U&E
• LFT
• ANA & Rheumatoid Factor
• PSA etc. led by history

Neutrophil count >15 x 10^9/L, persistent at 3 months & unexplained:
Refer to Haematology
Eosinophilia

Red Flag Signs
- If Eosinophil count > 2.5 look for signs of organ damage and consider urgent admission:
  - Venous Thromboembolism
  - Congestive Heart Failure
  - Gastrointestinal
  - Neurological
  - Pulmonary

If secondary cause found, treat as appropriate

Eosinophilia > 0.5 x 10⁹/L

Repeat FBC in 2 weeks and look for causes if > 1.5 (such as IgE level, Autoimmune Screen, Stool Cultures)

No cause found

Causes
- Asthma / atopic dermatitis / acute urticarial
- Infections: especially those due to parasites (most commonly helminthes - hookworm, schistosomiasis - but also giardiasis or other protozoal infections and strongyloides)
- Drugs (penicillins, carbamazepine, sulphamides are common but any drug is a possible cause)
- Connective tissue disease (rheumatoid arthritis, polyarteritis nodosa, Wegener's granulomatosis)
- Solid malignancy (breast, renal and lung cancer)
- Respiratory disease (Churg-Strauss syndrome, bronchiectasis, cystic fibrosis)
- Myeloproliferative disorders

If < 5.0 x 10⁹/L and persistent for 3 months
- Refer routinely to Haematology

If > 5.0 x 10⁹/L
- Refer urgently to Haematology

Patient Information TBC
Referral Proforma TBC
Local Guidance TBC
National Guidance TBC
Polycythaemia

High haematocrit (Hct) >0.51 in men, >0.48 in women

- Hct Male > 0.600, Female > 0.560 in the absence of congenital cyanotic heart disease
- Recent arterial or venous thromboembolism
- Neurological symptoms
- Visual Loss
- Abnormal bleeding

Refer to Haematology on urgent (suspected cancer) pathway

Does not meet criteria for urgent referral- repeat in 2 months and consider causes (see below)

If no obvious secondary cause and persistent, refer to Haematology routinely.

Causes
- Drugs – diuretics, testosterone, anabolic steroids
- Lifestyle choices - smoking, alcohol
- Hypoxia

Patient Information TBC
Referral Proforma TBC
Local Guidance TBC
National Guidance TBC
Thrombocytosis

Platelets >450 x 10^9/L

- Platelets >1000 x 10^9/L
- Recent arterial or venous thromboembolism
- Neurological symptoms
- Abnormal bleeding

Refer urgently (suspected cancer) to Haematology

Platelets >450 x 10^9/L

Refr FBC in 6 weeks and look for causes

If persistent >450 x 10^9/L and no obvious cause refer routinely to Haematology

Causes
- Iron Deficiency Anaemia
- Inflammation
- Infection
- Post-Splenectomy and Hyposplenism (e.g. Coeliac Disease)
- Myeloproliferative Disorders
- Post-Operatively
Thrombocytopenia

Thrombocytopenia

Platelets <150x10^9/L

Platelets <20
- Active Bleeding
- Blasts In Film
- Fragments In Film
- Altered Conscious Level Or Confusion

D/W on call Haematology to arrange urgent direct assessment

Platelets <50x10^9/LOR
- Associated with Cytopenias,
- Splenomegaly
- Lymphadenopathy
- Pregnancy
- Upcoming surgery

Repeat FBC in 1 week

Platelets >50x10^9/L

Repeat FBC in 6 weeks and look for causes

If persistent and unexplained refer to Haematology routinely

If platelets are less than 50x10^9/L please stop all antiplatelet agents and anticoagulation as unsafe to continue.

Please refer urgently to Haematology

Causes
- Spurious result from clumping – please look at blood film report and repeat using citrated sample
- Immune thrombocytopenic purpura (ITP)
- Alcohol
- Liver dysfunction
- Medications
- B12/folate deficiency
- HIV/Hepatitis B/C
- Bone marrow failure/infiltration

Platelets >50x10^9/L

Patient Information
TBC

Referral Proforma
TBC

Local Guidance
TBC

National Guidance
TBC
Paraprotein on Serum Protein Electrophoresis

End Organ Damage:
- Hypercalcaemia
- Unexplained renal impairment
- Anaemia or other cytopenias
- Bone pain or pathological fracture

Paraprotein <30
- SFLC ratio <8 or >0.1
- No Immunoparesis
- No End Organ Damage

Low Risk MGUS
- IgG <15
- IgM and IgA <10
- SFLC ratio <8 or >0.1
- No Organ Damage

Non-urgent referral to Haematology

High Risk MGUS
- IgG >15
- IgM and IgA >10

Urgent referral to Haematology

Any of following:
- Paraprotein >30
- SFLC ratio >8 or < 0.1
- Immunoparesis (low IgM/G/A)
- End Organ Damage
- Lymphadenopathy
- Splenomegaly

Urgent (suspected cancer) referral to Haematology

Note:
If there are concerns regarding the interpretation of paraprotein or Serum Free Light Chain results please discuss with the Haematology team.
Microcytic Anaemia

Hb <120g/L Woman
Hb <130g/L Man
AND
MCV <80

Is a thalassaemia / Hb variant likely?

Yes
Haemoglobinopathy testing advised

No

Hb abnormality found

A referral to the sickle cell and thalassaemia centre will be automatically generated

No Hb abnormality found

Possible alpha thalassaemia. If additional concern, discuss through advice and guidance

Rpt FBC, ferritin

Ferritin >50mcg/L

Possible Anaemia of chronic disease / inflammation

Refer to Haematology or through advice and guidance if no evidence of chronic disease / inflammation

Ferritin <30mcg/L
Or <50mcg/L with Iron sats <20%

?h/o menorrhagia, bowel symptoms, bleeding

Commence oral iron replacement

If cause unknown

If cause known

Check patient diet, TTG antibody, consider referral to gastroenterology for GI investigation / gynaecology. Patients with IDA DO NOT need to be referred to haematology

Treat underlying cause

National Guidance
TBC

Local Guidance
TBC

Referral Proforma
TBC

Patient Information
TBC
Normocytic or Macrocytic Anaemia

Hb <120g/L Woman
Hb<130g/L Man
AND
MCV >80

Check:
- FBC
- Blood Film
- UE/LFT
- TFT
- Vit B12
- Folate
- Ferritin
- Iron Saturations
- Reticulocyte count
- Serum Immunoglobulins
- Serum Free Light Chains

All tests normal or reticulocytes low or picture unclear

Paraprotein detected

Deranged renal function

Elevated reticulocyte count

Thyroid function abnormal

Ferritin <50mcg/L, low Vit B12 or Folate

Consider advice and guidance if not anaemia of chronic inflammation

Check calcium and suggest referral to Haematology for paraprotein investigation Exclude other causes of anaemia

Suggest referral to renal team

Look for evidence of bleeding or haemolysis and refer to appropriate department

Treat thyroid dysfunction and repeat testing 4-6 weeks

Suggest replace deficiency and assess for underlying cause

Note: Markers of haemolysis include a raised reticulocyte count and high bilirubin and LDH.
Macrocytosis

**Check**
- Alcohol history
- Medication (e.g. methotrexate, metformin, some anticonvulsants, hydroxycarbamide, antiretroviral drugs etc.)
- Blood Film
- Vit B12 and folate
- Reticulocyte count/LDH
- LFT
- TFT
- Serum immunoglobulins
- Serum Free Light Chains
- Family history

**Macrocytosis With/without anaemia**

**High Mean Cell Volume (MCV)**

Repeat FBC to ensure not spurious (e.g. delayed transport/ overheating etc.)

**MCV remains raised**

If Vit B12/folate deficient and Hb <80g/L or other cytopenias

Repeat FBC with reticulocyte count 5-7 days after starting replacement therapy

**Consider referral to Haematology if:**
- No secondary cause and MCV>105fL if other cytopenias or>110fL in the absence of other cytopenias
- No history of liver disease
- Dysplasia on blood film
- Paraprotein detected

**Notes**
*A high MCV can be a normal physiological finding in pregnancy*
Pancytopenia

Clinical assessment and assessment of severity

Severe if any of:
- Hb <80 g/L
- Neutrophils <0.5 x 10⁹/L
- Platelets < 30 x 10⁹/L

Consider reversible causes:
- Drugs e.g. methotrexate
- Haematinic deficiency
- Enlarged spleen

Check:
- Vit B12/folate
- Reticulocyte count
- U&E/LFT
- Bone profile
- Request blood film if not already available
- Immunoglobulins and serum free light chains

Non-severe
No clear cause

Routine referral to general Haematology clinic

Severe features present but clinically stable

Possible reversible cause

Blood film shows concerning features E.g. evidence of:
- DIC
- Blasts
- Leucoerythroblastic features

Clear cause

Treat underlying cause and monitor to ensure resolves

Follow advice from blood film report or discuss with on call Haematologists

Unwell/ febrile/ other clinical concerns

Discuss with on-call Haematologist Consider admission

2WW referral with close interim monitoring

Treat and discuss with Haematology team

No

Yes

Patient Information TBC

Referral Proforma TBC

Local Guidance TBC

National Guidance TBC
Hyperferritinaemia

Raised ferritin
> 400 μg/L male
> 200 μg/L female

Check
Repeat serum ferritin
Full Blood Count,
Liver Function Test,
Transferrin Saturation

If FBC abnormal & Tsat raised
(>50% male, 40% female)
Consider iron loading anaemia

If FBC is NORMAL &
Tsat is RAISED
(>50% male, 40% female)
Proceed to HFE genotyping*

If Tsat is NORMAL consider:
• Alcohol excess
• Inflammatory disorders
• Metabolic syndrome
• Malignancy

If Ferritin >1000mcg/L and normal iron sats
Refer to hepatology

Yes
Treat underlying cause and monitor to ensure resolves

No

If Ferritin <100mcg/L repeat in 6 months

*Note: it is recommended to screen ADULT first degree relatives (siblings) of known C282Y HOMOZYGOTES ONLY for genetic haemochromatosis due to their increased risk for C282Y homozygosity. Screening should be performed by iron studies and ferritin, with genetic testing reserved for those with abnormal results. HFE testing can be performed in primary care and does not require referral to haematology or clinical genetics (see text).

HFE testing in children is inappropriate as this is an adult onset condition.