Haematology for GP's

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Time to Learn, 03/07/2018

Anaemia

- Careful history (duration, symptoms, bleeding, diet, drug and family history)
- Blood film examination and reticulocyte count
- Ferritin, B12 and folate
- Immunoglobulins and protein electrophoresis

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-Acute haemolytic anaemia

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-Leukoerythroblastic anaemia

-Unexplained progressive *symptomatic* anaemia

- + splenomegaly /lymphadenopathy / other cytopenias

urgent haematology referral

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urgent haematology referral

- Persistent unexplained anaemia
- Iron deficiency showing sub-optimal response to oral iron therapy
- B12 deficiency of uncertain cause requiring further investigation

consider haematology referral

Neutropenia

- Neutrophil count < 1.7 x 10^9/l.
- (Africans/Afrocaribbeans normal range 1.0-7.0 x 109/l.

- Viral infection
- sepsis
- Drugs
- Autoimmune disorders
- Bone marrow failure (aplasia, malignant infiltration)
- B12/ folate deficiency

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- Neutrophil count < 1 x 10^9/l
- Neutropenia in association with

  - other cytopenia (Hb < 10g/dl, PLT < 50 x 10^9/l)

  -lymphadenopathy

  -splenomegaly

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urgent haematology referral

- Persistent (> 1 occasions 4-6 weeks apart), unexplained neutropenia 1-1.5 x 10^9/l

consider haematology referral

Thrombocytopenia

PLT < 150 x **10^9/l**
Risk of bleeding when < 20 x**10^9/l**

- ITP
- Bone marrow failure (Aplasia, malignant infiltration, MDS)
- Alcohol, Drugs
- Sepsis/ DIC/ hypersplenism
- B12/ folate deficiency
- TTP/ HUS

Thrombocytopenia

- Blood film examination – may exclude platelet clumping artefact
- B12 and folate levels
- Alcohol history
- Consider discontinuation of potentially precipitating medications
- Repeat FBC in 4-6 weeks

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- Platelet count < 50 x 10^9/l
- Platelet count 50 - 100 x 10^9/l in association with:
  - other cytopenia (Hb < 10g/dl, Neutrophils < 1 x 10^9/l)
  - splenomegaly or lymphadenopathy
  - pregnancy
  - upcoming surgery

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urgent haematology referral

- Persistent (>1 occasion 4-6 weeks apart, no clumping) unexplained thrombocytopenia < 80 x 10^9/l

consider haematology referral

Neutrophilia Leukocytosis

WCC > 10.5 X10 9/L

- Normal response to infection/ inflammation/ stress
- Haematological malignancy

Neutrophilia Leukocytosis

- Blood film examination with differential
- Careful history and assessment for 'reactive' causes (infection, inflammation, neoplasia)
- Examination for lymphadenopathy, splenomegaly
- Biochemistry
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New suspected CML with WCC >100 or hyperviscosity

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- Leucoerythroblastic blood picture
- New CML not meeting above criteria
- Unexplained leucocytosis with WCC 50 x 10^9/l)

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- Persistent (on >1 occasions 4-6 weeks apart) unexplained:
  - -White cell count >20 x 10^9/l
  - -Neutrophilia >15 x 10^9/l
  - -Eosinophilia / Monocytosis

consider haematology referral

Lymphocytosis

- Lymphocyte count > 4 x 10^9/l.
- A transient, reactive lymphocytosis is frequently seen in acute viral infection, particularly infectious mononucleosis.
- Chronic lymphocytosis is characteristic of chronic lymphocytic leukaemia (CLL), the incidence of which peaks between 60 and 80 years of age. In its early stages this condition is frequently asymptomatic with treatment only being required on significant progression.

Lymphocytosis

- Glandular fever screen, if appropriate
- Repeat FBC in 4-6 weeks: if lymphocytosis persists, a blood film will be normally reviewed by a Consultant Haematologist with a comment suggesting further action (e.g. "Please, refer, if clinically appropriate", "Forwarded for flow cytometry"e.t.c)

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- Lymphocytosis in association with:
  - anaemia, thrombocytopenia or neutropenia
  - splenomegaly
  - painful or progressive lymphadenopathy
  - B symptoms (weight loss >10%,soaking sweats,unexplained fever)

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Persistent lymphocytosis > 5 x not fulfilling criteria for urgent referral

(! please, discuss with a Haematologist)

consider haematology referral

Polycythaemia

-Primary proliferative polycythaemia (polycythaemia vera)
-Secondary causes (Hypoxic lung disease, erythropoietin-secreting tumours) ----
-Relative polycythaemia resulting from plasma depletion.

The threshold for therapeutic intervention with venesection or cytoreductive therapy in an individual patient depends on the cause, associated symptoms and thrombotic risk factors.

Polycythaemia

- Confirm with repeat FBC over time (uncuffed blood samples if possible)
- Modify known associated lifestyle factors (smoking, alcohol, consider changing thiazides to non-diuretic antihypertensive agents)

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- Hb>20g/dl (PCV >0.60) in the absence of chronic hypoxia
- Raised Hb in association with:
  - recent arterial or venous thrombosis
  - neurological symptoms
  - visual loss
  - abnormal bleeding

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- Persistent (at least on two occasions 4-6 weeks apart) unexplained eleveted PCV (male >0.52, female >0.48)
- Elevated PCV (male >0.52, female >0.48) in association with
  - past history of arterial or venous thrombosis
  - splenomegaly
  - pruritus
  - elevated WCC or PLT

consider haematology referral

Thrombocytosis

PLT > 450 x 10^9/l

- Primary myeloproliferative disorder (essential thrombocythaemia) or
- ‘Reactive’: (infection, inflammation, chronic bleeding or neoplasia)

Very high platelet counts in the setting of myeloproliferative disorders carry risk of both thrombosis and abnormal bleeding (due to platelet dysfunction).

Thrombocytosis

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- Look for and treat reactive causes (infection, inflammation, neoplasia)

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- PLT 600 – 1000 x 10^9/l in association with:
  - -recent arterial or venous thromboembolism
  - -neurological symptoms
  - -abnormal bleeding

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urgent haematology referral

- Persistent (on >1 occasions 4-6 weeks apart) unexplained PLT > 600 x 10^9/l
- PLT 450-600 x 10^9/l in association with
  - - past history of arterial or venous thrombosis
  - - splenomegaly
  - - pruritus
  - - elevated Hb or WCC

consider haematology referral

Paraproteinaemia

- MGUS is a diagnosis of exclusion: 3% of over the age of 70 and 5% of over the age of 80 have a paraprotein which is frequently found incidentally and not associated with symptoms or physical findings. The overall risk of MGUS progression to myeloma is around 1% per year – this remains constant over time.
- *Referrals to Haematology should not be made for patients with raised immunoglobulin levels in the absence of a paraprotein band on serum electrophoresis.*

Paraproteinaemia

suspected spinal cord compression

contact on-call haematologist

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Any new paraprotein plus:

- hypercalcaemia
- unexplained renal impairment or urinary Bence Jones proteins
- bone pain or pathological fracture
- radiological lesions reported as suggestive of myeloma
- anaemia or other cytopenia
- hyperviscosity symptoms (headache, visual loss, acute thrombosis)

urgent haematology referral

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urgent haematology referral

Other newly identified paraproteins not meeting above criteria

consider haematology referral

Lymphadenopathy

- FBC, blood film
- Biochemistry
- Glandular fever screen
- Consider CXR

- Lymphadenopathy >1cm persisting for >6 weeks with no obvious infective precipitant
- Lymphadenopathy for <6 weeks in association with:

-B symptoms (weight loss >10%, soaking sweats, unexplained fever)

-hepatic or splenic enlargement

-rapid nodal enlargement

-disseminated / generalised nodal enlargement

-anaemia / leucopenia / thrombocytopenia

-hypercalcaemia

urgent haematology referral

Night sweats

- Common presenting symptom in primary care practice
- Often difficult to distinguish from hot flashes
- No published recommendations for evidence-based approach

Night sweats

Malignancy	Substance withdrawal	Medications
Lymphoma	Alcohol	**Miscellaneous**
Solid tumors	Cocaine	Chronic fatigue syndrome
Germ cell tumors	Opioids	Food additives
Medullary carcinoma thyroid	**Endocrine disorders**	Gastroesophageal reflux
Prostate cancer	Carcinoid syndrome	Mastocytosis
Renal cell carcinoma	Pheochromocytoma	Panic disorder
Insulinoma	**Hyperthyroidism**	Rosacea
Infections	Hypoglycemia	Sleep apnea
TB	Diabetes insipidus	Tempral arteritis
Atypical mycobacteria	Postorchiectomy	Idiopathic hyperidrosis
Abscess	**Menopause**	
Brucellosis	**Neurologic disorders**	
Endocarditis	Autonomic dysrefleia	
Osteomyelitis	Autonomic neuropathy	
HIV	Post-traumatic syringomyelia	
Chronic hepatitis C	Stroke	

Night sweats

Antidepressants	Hypoglycemic agents	Miscellaneous (cont)
Bupropion	Insulin	Interferon alpha-2b
SSRIs	Sulfonylureas	Morphine
SSNRIs	Thiazolidinediones	Niasin
Tricyclic antidepressants	**Sympathomimetic agents**	Nitroglycerin
Anti-migraine drugs	Beta-agonists	Omeprazole
‘Triptans’’ serotonin 5-HT agonists	Phenylephrine	Opioids
Antipyretics	**Miscellaneous**	Protease inhibitors
Acetaminophen	Alcohol	Rituximab
Aspirin	Beta blockers	Ropinirole
NSAIDs	Calcium channel blockers	Sildenafil
Cholinergic agonists	Chlozapine	Theophylline
Pilocaprin	Cyclosporine	Tramadol
Pyridostigmin	Donepezil	
Hormonal agents	Fluvoxamine	
GnRH agonists	Hydralazine	
Aromatase inhibitors (letrozole)	Imatinib	
SERMs (Tamoxifen)	Infliximab	

Night sweats

History:

- Exclude fever, look for associated symptoms
- Unintentional weight loss+ lymphadenopathy , pruritus -> ? Lymphoma
- Back pain + fever +new murmur -> ? endocarditis
- Fever + localized pain -> abscess
- Rigors-> bacterial infection
- Risk factors for HIV
- Medication history (prescription+ over-the-counter medications)
- Flushing, diarrhea, headcahe, heat intolerance, tremor-> ? Endocrine cause

Night sweats

Physical examination:

- Temperature, heart rate, blood pressure, weight.
- Skin examination (sweating pattern, flushing, stigmata of endocarditis)
- Abnormal lymphadenopathy, splenomegaly
- Lid lag
- Murmurs

Night sweats

Diagnostic strategy

- Discontinue medication if known to cause flushing or excessive sweating
- Drenching night seats that require changing bedclothes

  - Chest X-ray

  -TSH

  -HIV testing

  -FBC

  -Blood cultures

  -CT scan

  -Bone marrow biopsy

- If diagnosis remains elusive check 5-HIAA, catecholamines, FSH

Suspected Haemochromatosis

- Over 90% of cases are caused by homozygous (C282Y) mutation of the HFE gene which can be detected by PCR
- *A raised ferritin may also be reactive to other conditions, particularly other causes of liver disease, alcohol excess, infection, inflammation or neoplastic disease.*

Suspected Haemochromatosis

- Repeat ferritin measurement in 4-6 weeks
- Check LFT, fasting glucose, transferrin saturation
- Careful alcohol history
- Consider 'reactive' cause: infection, inflammation, neoplasia

Elevated ferritin with evidence of otherwise unexplained 'end organ damage'

(CCF, liver dysfunction, diabetes, hypogonadism)

urgent haematology referral

- Persistent unexplained ferritin >600 mcg/L, and/or transferrin saturation >50%.
- Genetic counselling/screening of first degree relatives of hereditary haemochromatosis cases

consider haematology referral

CLL and Low Grade Lymphoma –Discharge advice

- **Monitor FBC annually**
- **Reasons to re-refer:**

• Lymphocyte count rising rapidly (typically doubling within 6 months)
• Lymphocyte count rising above 100 109/l
• Developing a significant cytopenia (Hb<10, neutrophils <1.5, PLT <80):
• Developing significant 'B' symptoms
    Weight loss unexplained (Greater than 3kg in 3 months)
    Drenching night sweats
    PUO (documented)
• Recurrent infections
• Clinical Examination:
    -Lymph nodes alone or in groups (>5 cm diam or >3 sites with >3 cm diam)
    -Spenomegaly > 16cm or >4cm below left costal margin
    -Bone lesions
    -Renal impairment
    -Pleural effusion (new)
    -Hepatomegaly/ jaundice

THROMBOCYTOPENIA – Discharge advice

- **Advice is for patients with long term, stable ITP**

  (PLT stable > 30 10x9/l for greater than 18 months)

- Monitor FBC annually, or

  at any point when unexpected bruising/bleeding.

- Reasons to re-refer:
  - PLT <20 109/l
  - Developing a significant cytopenia (Hb<10, neutrophils<1.5 or PLT <80)
  - Pregnancy

Monitoring of MGUS

- **Advice applies to very low risk patients with MGUS:**

  IgG band <15 g/L and normal Free Light Chains

- Monitor FBC, U&E, Creatinine and Ca++ and Serum Electrophoresis annually
- Dipstick urine for protein annually
- Reasons to re-refer:
  - • Monoclonal Band rising unexpectedly (>50% increase compared to baseline)
  - • Developing a significant cytopenia (Hb <10 g/dl; Neutrophils <1.5 x 109/l, PLT < 80 109/l)
  - •Developing renal impairment
  - Severe proteinuria with 24 hr proteins >1,5g/day or ++/+++ on Dip stick examination.
  - • Unexplained hypercalcaemia
  - • Pathological fracture or unexplained bone pain
  - • Lymph nodes enlargement with >3 lymph nodes >3 cm diameter
  - • Unexplained weight loss > 3 kg within <3 months of time.

Visit the website

http://www.southend.nhs.uk/media/22256/referralguidelineshaematology.pdf

Thank you