ST. VINCENT'S UNIVERSITY HOSPITAL
Elm Park

ST. VINCENT'S HEALTHCARE GROUP
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Haematology Department

Referral Guidance/Timelines

October 2023

Referral Guidance / Timelines

Immediate *	Within Hours
Very Urgent *	Within 48hrs
Urgent	Within 2 weeks
Routine	Within 18 weeks

(* Discuss with Haematology Consultant on Call pre Referral)

Waiting time starts from when the hospital or service receives referral letter.

During this time period, the clinician reviewing the referral may:

- Organise blood tests, scans or other procedures to help ensure that your treatment is appropriate for your condition

- be referred to another consultant or department

Your waiting time ends if a clinician decides no treatment is necessary, if you decide you do not want to be treated, or when your treatment begins.

Guidelines

1. Anaemia
2. Macrocytosis
3. Vitamin B12
4. Leucocytosis
5. Neutropenia
6. Lymphocytosis
7. Lymphopenia
8. Eosinophilia
9. Thrombocytosis
10. Thrombocytopenia
11. Polycythaemia
12. Raised Vitamin B12
13. Lymphadenopathy
14. Sweats
15. Splenomegaly
16. Paraprotein
17. VTE
18. Abnormal Coagulation results
19. Easy bruising/bleeding

1. Anaemia

Hb <13.0 gm/dl in males; <11.5 gm/dl in females:
The patient's symptoms and initial FBC, MCV and blood film features will influence both the urgency and direction of initial clinical investigation.

Important: Iron deficiency should generally be referred to gastroenterology / gynaecology / urology as appropriate for further investigation.

Suggested test in primary care:

- Careful history focussing on duration, symptoms, bleeding, diet, drug and family history •Blood film and reticulocyte count
- Ferritin, Vitamin B12, folate (Iron studies may be more useful than ferritin if there is an inflammatory component)
- Immunoglobulins, serum protein electrophoresis, serum free light chains
- Renal and liver function
- ESR (if clinically indicated) and CRP
- Autoimmune screen to exclude chronic inflammation

Criteria for URGENT referral (Out-patient criteria):

- Leucoerythroblastic anaemia (based on blood film)
- Anaemia with dysplastic features (based on blood film)
- Anaemia with reticulocytosis (No bleeding)
- Unexplained progressive **symptomatic** anaemia
- Anaemia in association with: splenomegaly or lymphadenopathy or other cytopenias.

Criteria for ROUTINE referral:

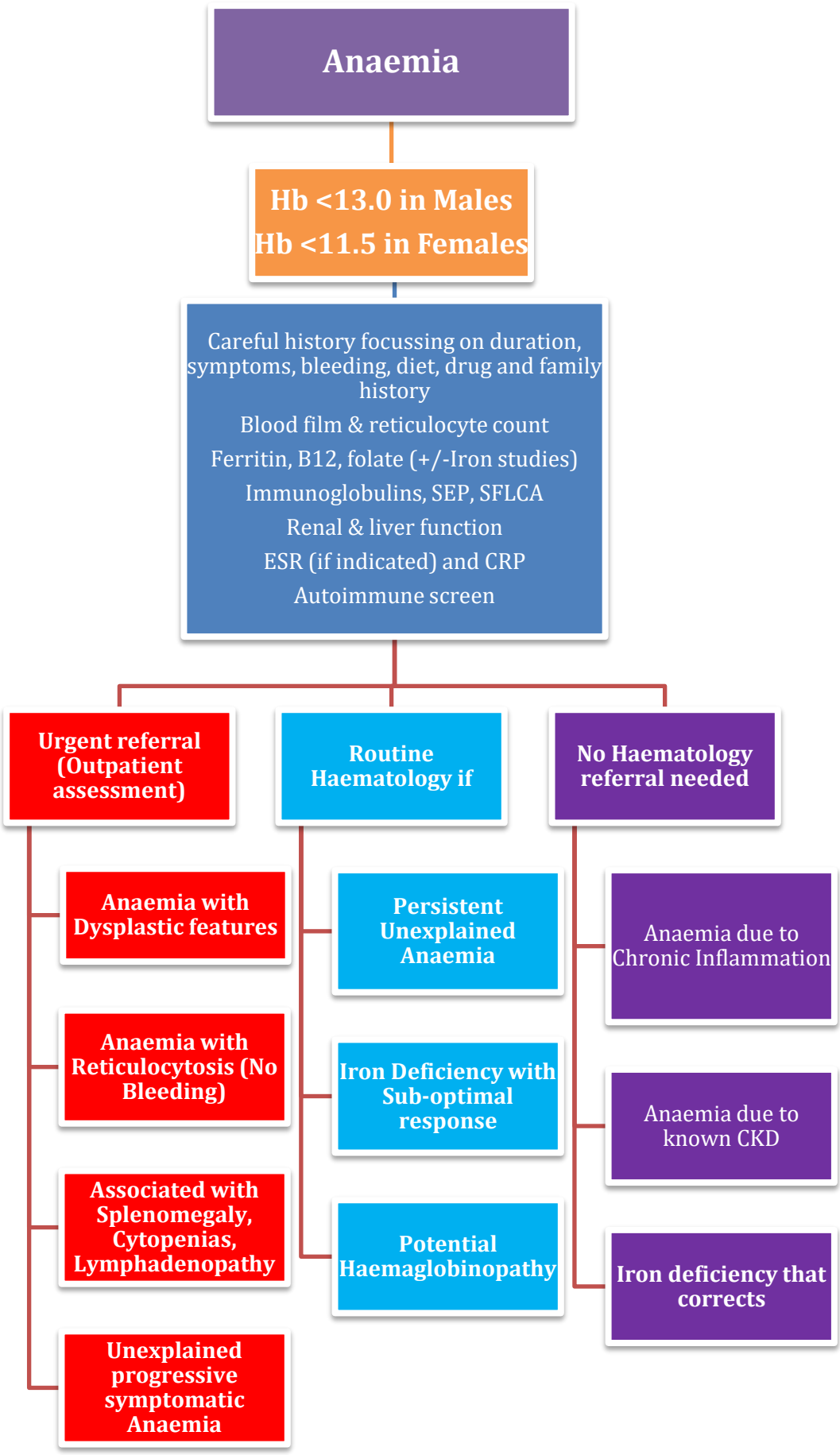
- Persistent unexplained anaemia
- Iron deficiency with sub-optimal response to oral iron (Ferrous fumarate 305mg alternate daily) after a 2-3 month trial of iron
- Patients intolerant of a single preparation of oral iron should be switched to an alternative as they may tolerate them better.
- The primary investigation of the iron deficiency e.g. gasteroenterology, gynaecology or urology should be carried out by the appropriate referrals in primary or secondary care.

Potential Haemaglobinopathy:

- Consider potential Haemaglobinopathy in patients of appropriate ethnic variation with isolated microcytosis and/or elevated RCC
- Check serum ferritin prior to Iron replacement, even in the presence of microcytosis

Who does not need referral to Haematology:

- Anaemia due to chronic inflammation or known chronic kidney disease
- Iron deficiency anaemia that corrects with iron replacement and management of losses when cause clear.


Anaemia
Hb <13.0 in Males
Hb <11.5 in Females
Careful history focussing on duration, symptoms, bleeding, diet, drug and family history
Blood film & reticulocyte count
Ferritin, B12, folate (+/-Iron studies)
Immunoglobulins, SEP, SFLCA
Renal & liver function
ESR (if indicated) and CRP
Autoimmune screen
Urgent referral (Outpatient assessment)
Routine Haematology if
No Haematology referral needed
Anaemia with Dysplastic features
Anaemia with Reticulocytosis (No Bleeding)
Associated with Splenomegaly, Cytopenias, Lymphadenopathy
Unexplained progressive symptomatic Anaemia
Persistent Unexplained Anaemia
Iron Deficiency with Sub-optimal response
Potential Haemaglobinopathy
Anaemia due to Chronic Inflammation
Anaemia due to known CKD
Iron deficiency that corrects

2. Macrocytosis

Elevated MCV >100 fl:
The differential diagnosis of red cell macrocytosis includes vitamin B12 and folate deficiency, excess alcohol consumption, hypothyroidism, reticulocytosis and myelodysplastic syndrome.
Macrocytosis can be a normal physiological finding in pregnancy and it is seen routinely in patients taking either hydroxyurea (hydroxycarbamide), methotrexate or certain antiretroviral agents. It can also be seen when there is a delay in transport of sample to the laboratory.

Suggested test in primary care:

- Repeat FBC testing to ensure not spurious e.g. delayed transport/overheating of sample
- Vitamin B12 and folate levels (plus Intrinsic Factor Antibodies and coeliac screen if low)
- Blood film examination and reticulocyte count
- Liver and thyroid biochemistry
- Alcohol history and appropriate lifestyle modification
- Assess alcohol intake (check GGT)
- Protein electrophoresis / immunoglobulins / urine for Bence-Jones protein
- Review medications

Criteria for URGENT referral (Out-patient criteria):

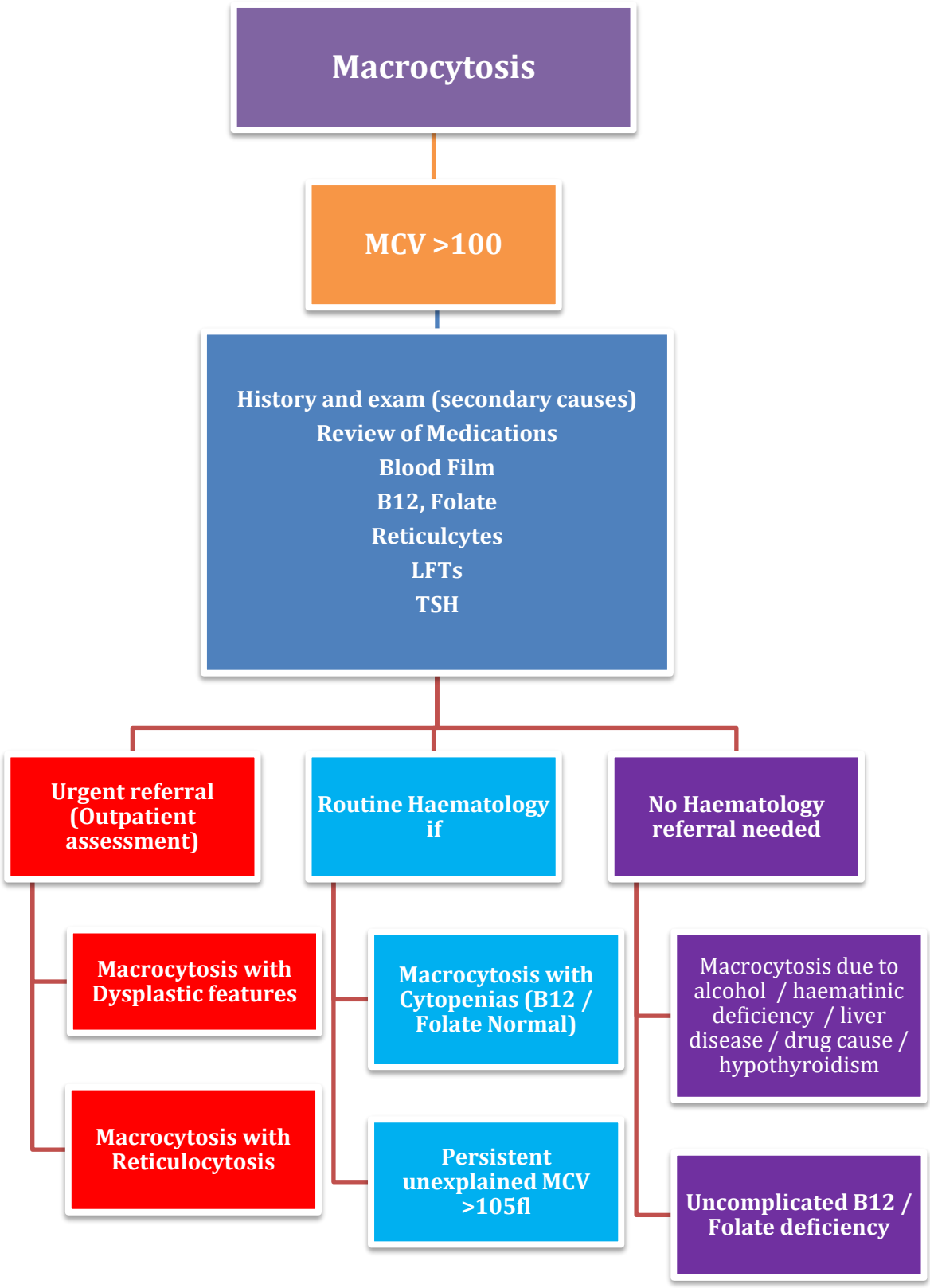
- Macrocytosis with dysplastic features on a blood film (suggested on a film comment, raising suspicion for myelodysplastic syndrome)
- Macrocytosis with increased reticulocytes (raising suspicion for haemolysis)

Criteria for ROUTINE referral:

- MCV > 100fl with accompanying cytopenia (excluding vitamin B12 / folate deficiency)
- Persistent unexplained MCV > 105fl

Who does not need referral to Haematology:

- Macrocytosis due to alcohol excess / haematinic deficiency if corrects on replacement / liver disease / drug cause / hypothyroidism (should normalize on treatment)
- Uncomplicated vitamin B12 or folate deficiency does not require referral to haematology.


Macrocytosis
MCV >100
History and exam (secondary causes)
Review of Medications
Blood Film
B12, Folate
Reticulcytes
LFTs
TSH
Urgent referral (Outpatient assessment)
Routine Haematology if
No Haematology referral needed
Macrocytosis with Dysplastic features
Macrocytosis with Reticulocytosis
Macrocytosis with Cytopenias (B12 / Folate Normal)
Persistent unexplained MCV >105fl
Macrocytosis due to alcohol / haematinic deficiency / liver disease / drug cause / hypothyroidism
Uncomplicated B12 / Folate deficiency

3. Vitamin B12 Deficiency

Causes of B12 Deficiency:
• Pernicious anaemia
• Gastrectomy
• Inadequate dietary intake – vegan diet
• Malabsorption
• Ileal resection
• Crohn's disease
• Colchicine, metformin, long term use of PPIs
• Food based malabsorption associated with gastric atrophy either age related or associated with long term PPI

Pregnancy and Low B12 levels:

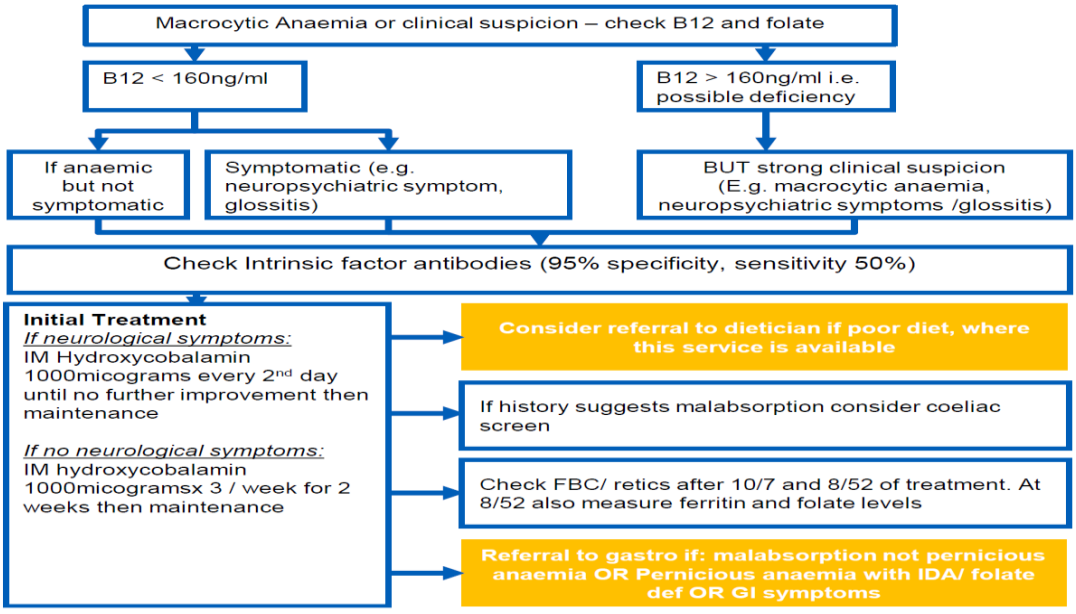
- Serum vitamin B12 levels fall in pregnancy. The physiological reduction can be up to 50%. Levels return to normal rapidly after delivery without supplementation.
- Vitamin B12 demands increase in pregnancy, but normal body stores last up to 5 years, resulting in deficiency in pregnancy being relatively uncommon.
- There is an absence of pregnancy specific reference ranges, so results should be interpreted with caution. Ideally levels should only be checked if there is a high suspicion

HRT & Oral Contraceptive Pill:

- These therapies can result in a low vitamin B12 level that does not require further investigation and treatment unless a strong clinical suspicion of vitamin B12 deficiency

Type 2 Diabetes and on Metformin:

- No definitive advice can be given on the desirable frequency of monitoring of serum vitamin B12. It should be checked if strong clinical suspicion of deficiency.
- If vitamin B12 levels low, anti–Intrinsic Factor Ab should be checked.
  • If positive, administer lifelong treatment with hydroxycobalamin.
  • If negative, the reduced level may be purely as a result of metformin, although underlying ab negative pernicious anaemia cannot be excluded. Treatment with oral cobalamin (50microgram for 1 month) may be considered; subsequent monitoring of vitamin B12 levels at 6 months and then yearly intervals is suggested



4. Leucocytosis

Elevation of white cell count >11 x 10^9/l:
Secondary or reactive causes are more common causes of leucocytosis. The most common causes are normal responses to acute infection or inflammation or acute stress (acute bleed, ACS). Other common causes include smoking and steroid use. Primary causes e.g. acute or chronic leukaemia are rare.

Suggested test in primary care:
- History and physical examination (clue to secondary or 'reactive' causes)
- Differential white cell count (see separate criteria for lymphocytosis and eosinophilia)
- Assessment for presence of lymphadenopathy or splenomegaly
- Renal/Liver and bone bloods
- Ferritin and iron studies
- CRP
- Urinalysis and CXR

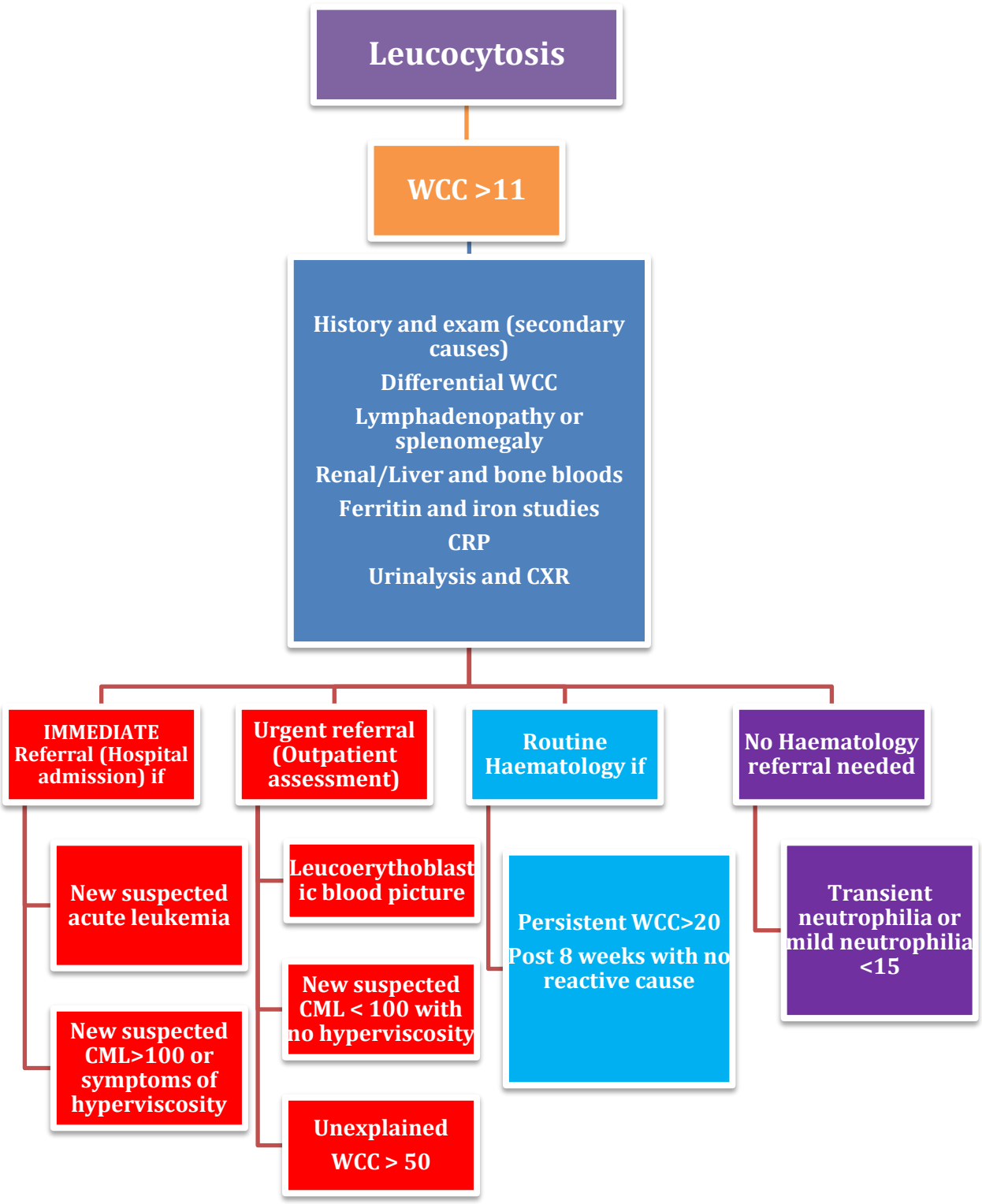
Criteria for IMMEDIATE* referral (Hospital admission):
- New suspected acute leukaemia
- New suspected chronic myeloid leukaemia (CML) with either WCC >100 or symptoms of hyperviscosity (headaches/visual disturbance/thrombosis)

(* Discuss with Consultant Haematologist on call pre-referral)

Criteria for URGENT referral (Out-patient criteria):
- Leucoerythoblastic blood picture
- New suspected CML with WCC < 100 with no hyperviscosity
- Unexplained WCC > 50

Criteria for ROUTINE referral:
- Persistent WCC>20 after 8 weeks with no reactive cause

Who does not need referral to Haematology:
- Transient neutrophilia or mild neutrophilia <15


Leucocytosis
WCC >11
History and exam (secondary causes)
Differential WCC
Lymphadenopathy or splenomegaly
Renal/Liver and bone bloods
Ferritin and iron studies
CRP
Urinalysis and CXR
IMMEDIATE Referral (Hospital admission) if
Urgent referral (Outpatient assessment)
Routine Haematology if
No Haematology referral needed
New suspected acute leukemia
New suspected CML>100 or symptoms of hyperviscosity
Leucoerythoblastic blood picture
New suspected CML < 100 with no hyperviscosity
Unexplained WCC > 50
Persistent WCC>20
Post 8 weeks with no reactive cause
Transient neutrophilia or mild neutrophilia <15

5. Neutropenia

Isolated neutrophil count <1.5 x 10^9/L:
Review ethnicity of all patients. A neutrophil count between 1-2 x 10^9/L is normal in people of West-African, Afro-Caribbean and Middle Eastern ancestry.
The most common cause of neutropenia is viral infection and medications.
Patients with mild neutropenia (1-1.8 x 10^9/L) are not generally at risk of infection

Suggested test in primary care:

- Assess ethnicity
- History (recurrent infections/mouth ulcers/thrush)
- Examination (lymphadenopathy and splenomegaly)
- Repeat FBC
  -if neutrophils >1 x 10^9/L, repeat in 6 weeks
  -if neuts <1 x 10^9/L, repeat in 1 week
- If neutropenia persists
  -Blood film
  -Ferritin/Iron studies/Vit B12/Folate
  -Renal, liver and bone profile and LDH
  -HIV, Hep B and Hep C serology
  -ANA

Criteria for IMMEDIATE referral:
Neutrophil count of <1 x 10^9/L post chemotherapy and evidence of sepsis
Neutrophil count of <0.5 x 10^9/L consider admission if new finding and clinical concern

Criteria for URGENT referral (Out-patient assessment):

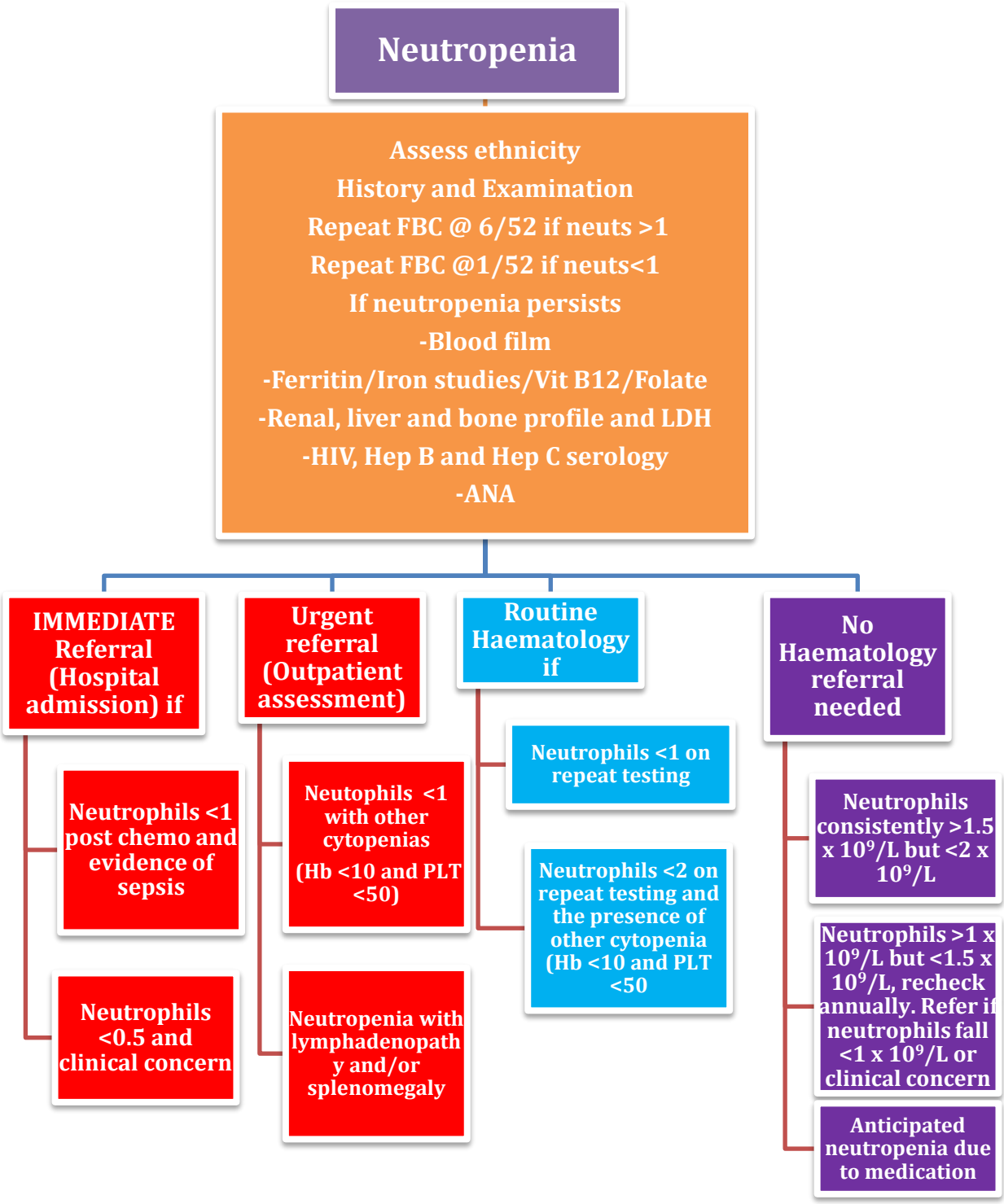
- Neutropenia <1 x 10^9/L associated with other cytopenias (Hb <10 g/dL and PLT <50 x 10^9/L unless established liver disease)
- Neutropenia associated with lymphadenopathy and/or splenomegaly

Criteria for ROUTINE referral:

- Neutropenia <1 x 10^9/L on repeat testing
- Neutropenia <2 x 10^9/L on repeat testing and the presence of other cytopenia (Hb <10 g/dL and PLT <50 x 10^9/L)

Who does not need referral to Haematology:

- Neutrophils persistently >1.5 x 10^9/L but <2 x 10^9/L. No further monitoring required if sustained and patient well.
- Neutrophils >1 x 10^9/L but <1.5 x 10^9/L, recheck annually. Refer if neutrophils fall <1 x 10^9/L or clinical concern.
- Anticipated neutropenia due to medication
- Neutropenia associated with infection. Repeat once infection has resolved and if consistently <1 x 10^9/L, can refer


Neutropenia
Assess ethnicity
History and Examination
Repeat FBC @ 6/52 if neuts >1
Repeat FBC @1/52 if neuts<1
If neutropenia persists
-Blood film
-Ferritin/Iron studies/Vit B12/Folate
-Renal, liver and bone profile and LDH
-HIV, Hep B and Hep C serology
-ANA
IMMEDIATE Referral (Hospital admission) if
Neutrophils <1 post chemo and evidence of sepsis
Neutrophils <0.5 and clinical concern
Urgent referral (Outpatient assessment)
Neutophils <1 with other cytopenias (Hb <10 and PLT <50)
Neutropenia with lymphadenopathy and/or splenomegaly
Routine Haematology if
Neutrophils <1 on repeat testing
Neutrophils <2 on repeat testing and the presence of other cytopenia (Hb <10 and PLT <50
No Haematology referral needed
Neutrophils consistently >1.5 x 10⁹/L but <2 x 10⁹/L
Neutrophils >1 x 10⁹/L but <1.5 x 10⁹/L, recheck annually. Refer if neutrophils fall <1 x 10⁹/L or clinical concern
Anticipated neutropenia due to medication

6. Lymphocytosis

Lymphocyte count above laboratory reference range (> 4.0 x 10^9/L):
A transient reactive lymphocytosis is common and can be seen in acute viral infections (particularly infectious mononucleosis), acute chest pain, status epilepticus etc. Smoking is a well-recognised cause of a reactive lymphocytosis and is often associated with mild neutrophilia and monocytosis.

Chronic lymphocytosis is characteristic of CLL and can be seen in other lymphoproliferative disorders. In the early stages, these conditions are frequently asymptomatic, with treatment only required on significant progression. Many with chronic lymphoproliferative disorders may never require treatment throughout their lifetime.

Suggested tests in primary care:

- Blood film if lymphocytes persistently > 5 x 10^9/l on repeat testing
- Monospot test and inflammatory markers
- LFTs
- Repeat FBC in 8 weeks if lymphocyte count 6-10 x 10^9/l (viral lymphocytosis is frequently transient)
    - If persistent
        - Viral serology for EBV / CMV / HIV / hepatitis B and C (if relevant symptoms)
        - Immunophenotyping if lymphocytes are > 6 x 10^9/l for >2 months. Please send 1 x EDTA sample to lab.
- Lifestyle modifications e.g. Smoking Cessation

Criteria for URGENT Referral to Haematology:

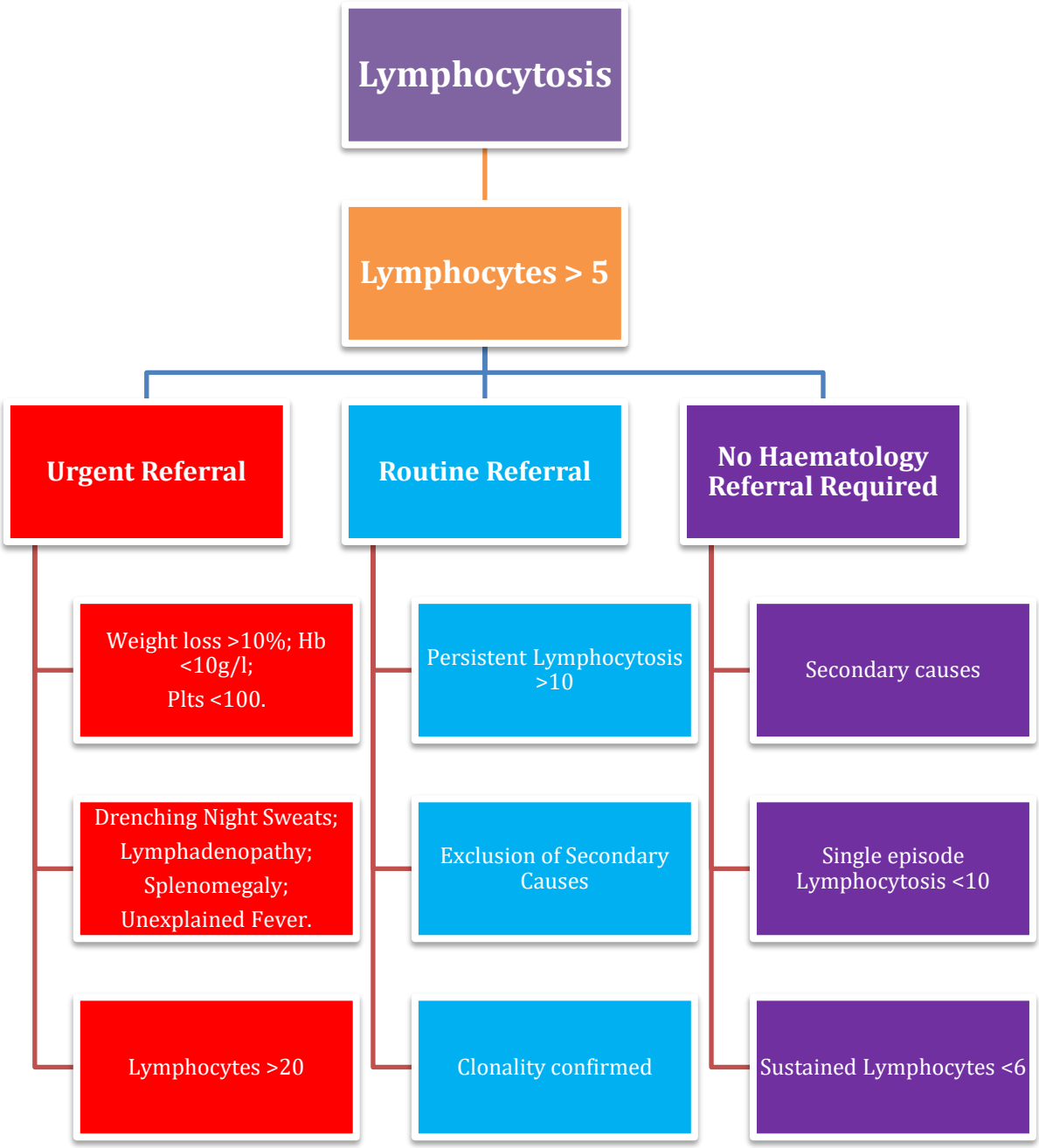
- Lymphocytosis in association with
    - Anaemia (Hb <10g/l)
    - Thrombocytopenia (Platelets < 100 x 10^9/l) or
    - Neutropenia (Neutrophils <1.0 x 10^9/l)
- Symptomatic patients
    - Weight loss (>10% in 6mth), fever, drenching night sweats),
    - Palpable lymphadenopathy >1cm and / or splenomegaly
- Lymphocytosis in > 20 x 109/l (or rapidly increasing)

Criteria for ROUTINE referral:

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

Who does not need referral to Haematology:

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


Lymphocytosis
Lymphocytes > 5
Urgent Referral
Routine Referral
No Haematology Referral Required
Weight loss >10%; Hb <10g/l;
Plts <100.
Drenching Night Sweats;
Lymphadenopathy;
Splenomegaly;
Unexplained Fever.
Lymphocytes >20
Persistent Lymphocytosis >10
Exclusion of Secondary Causes
Clonality confirmed
Secondary causes
Single episode Lymphocytosis <10
Sustained Lymphocytes <6

7. Lymphopenia

Lymphocyte count below laboratory reference range (< 1.0 x 10^9/l):
Lymphopenia is a common, non-specific finding. Its significance should be judged in light of age, clinical details and other results.

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

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

Suggested tests in primary care:

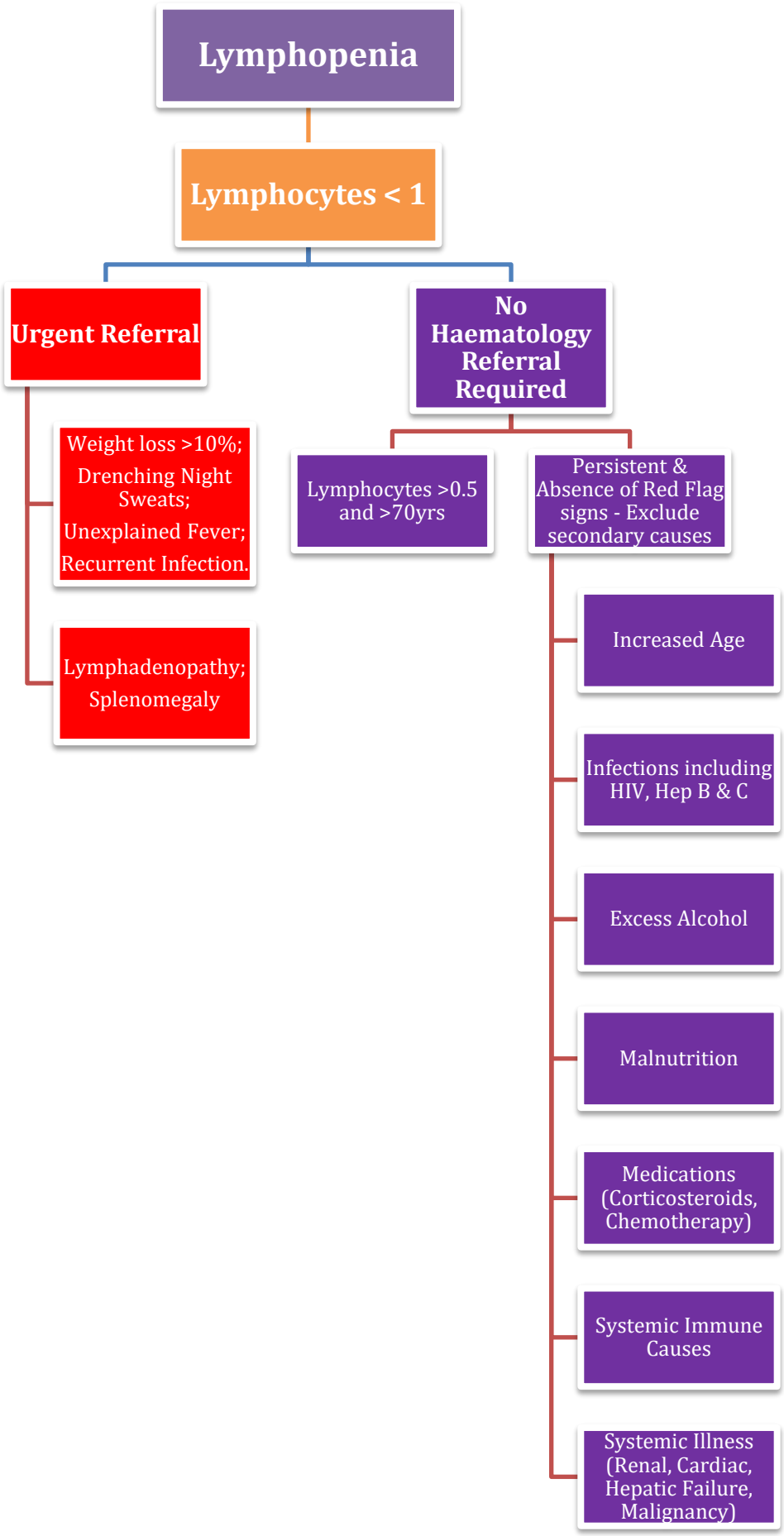
- Blood film
- Renal and hepatic function
- ANA
- HIV & Hepatitis serology
- Immunoglobulins and serum electrophoresis

Criteria for ROUTINE referral:

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

Who does not need referral to Haematology:

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


Lymphopenia
Lymphocytes < 1
Urgent Referral
No Haematology Referral Required
Weight loss >10%; Drenching Night Sweats; Unexplained Fever; Recurrent Infection.
Lymphadenopathy; Splenomegaly
Lymphocytes >0.5 and >70yrs
Persistent & Absence of Red Flag signs - Exclude secondary causes
Increased Age
Infections including HIV, Hep B & C
Excess Alcohol
Malnutrition
Medications (Corticosteroids, Chemotherapy)
Systemic Immune Causes
Systemic Illness (Renal, Cardiac, Hepatic Failure, Malignancy)

8. Eosinophilia

Elevation of eosinophils above 0.5 x 10^9/l:
Eosinophilia is usually reactive. Secondary causes include infection (parasitic and fungal infection), allergy, asthma, connective tissue disorders and malignancy.
There are three main categories of eosinophilia - secondary causes, primary clonal eosinophilia and idiopathic

Suggested tests in primary care:

- Travel history, allergic reactions, medication history
- FBC and blood film
- Renal, liver and bone profile and LDH
- CRP and ESR
- Vit B12
- CXR and urinalysis (proteinuria)
- Vasculitis screen
- Stool for Ova, cysts and parasites

Criteria for URGENT referral:

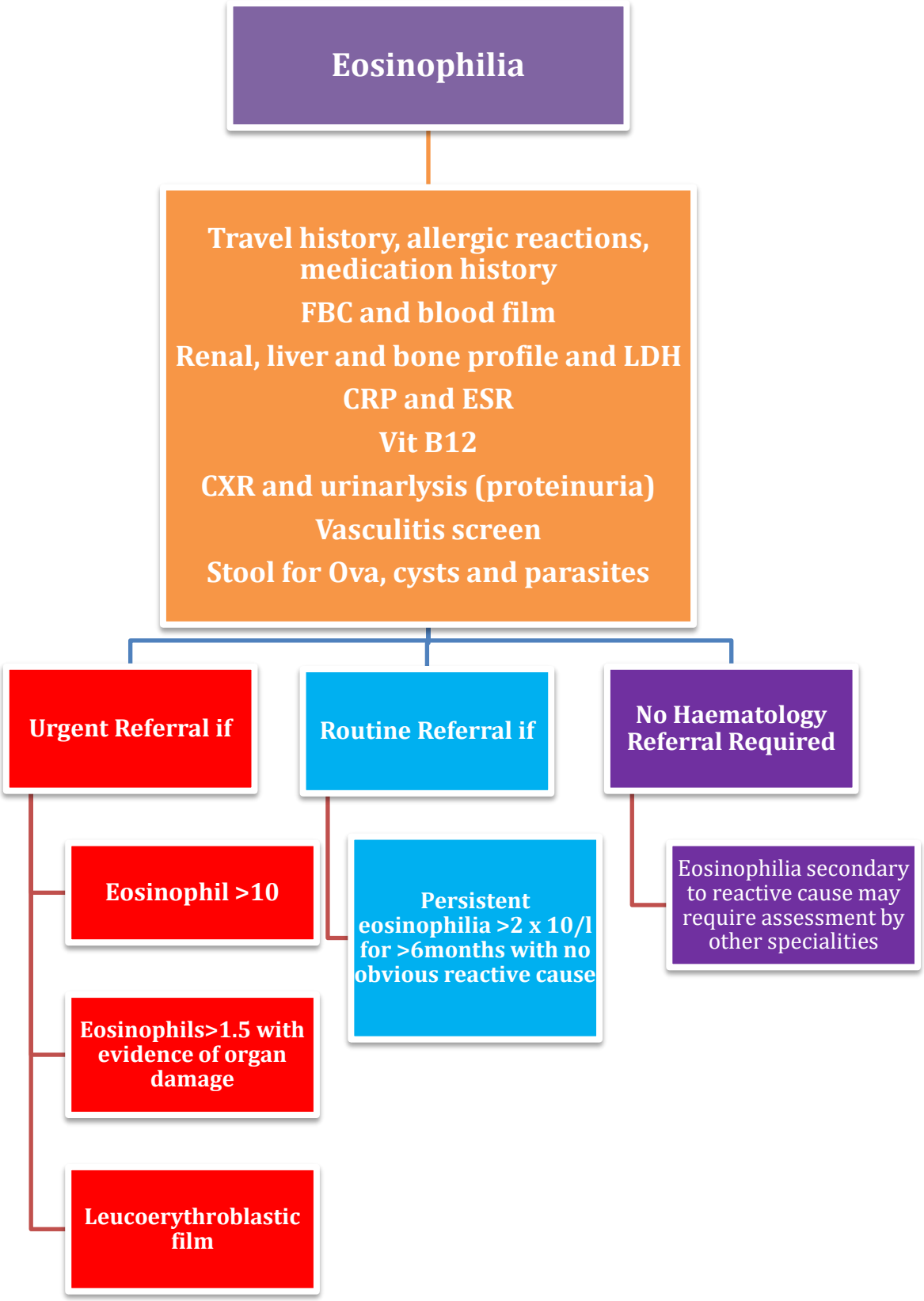
- Eosinophil >10
- Eosinophils>1.5 with evidence of end organ damage
- Leucoerythroblastic film

Criteria for ROUTINE Referral:

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

Who does not need referral to Haematology:

- Eosinophilia secondary to reactive cause may require assessment by other specialities


Eosinophilia
Travel history, allergic reactions, medication history
FBC and blood film
Renal, liver and bone profile and LDH
CRP and ESR
Vit B12
CXR and urinarlysis (proteinuria)
Vasculitis screen
Stool for Ova, cysts and parasites
Urgent Referral if
Routine Referral if
No Haematology Referral Required
Eosinophil >10
Eosinophils>1.5 with evidence of organ damage
Leucoerythroblastic film
Persistent eosinophilia >2 x 10/l for >6months with no obvious reactive cause
Eosinophilia secondary to reactive cause may require assessment by other specialities

9. Thrombocytosis

Defined as persistent increase in platelet count over **450 x 10/^{9}l:**

Secondary or reactive causes are more common than primary bone marrow disorders (myeloproliferative neoplasms).
The most common secondary (or reactive) causes of thrombocytosis are infection, inflammation and iron deficiency.
Other causes include tissue damage, haemolysis, severe exercise, malignancy and hyposplenism / Post splenectomy.
Primary causes are more suggestive if there is an accompanying erythrocytosis or leucocytosis, arterial or venous thrombotic events or abnormal bleeding when platelet count is high (due to platelet dysfunction).

Fluctuating thrombocytosis is more suggestive of secondary / reactive cause.

Suggested test in primary care:

- History and examination (clues to iron deficiency or reactive causes)
- Serial FBCs (over 3 months apart)
- CRP and ANA
- Ferritin/Iron studies
- Renal and liver function
- Vitamin B12/Folate

Criteria for URGENT referral:

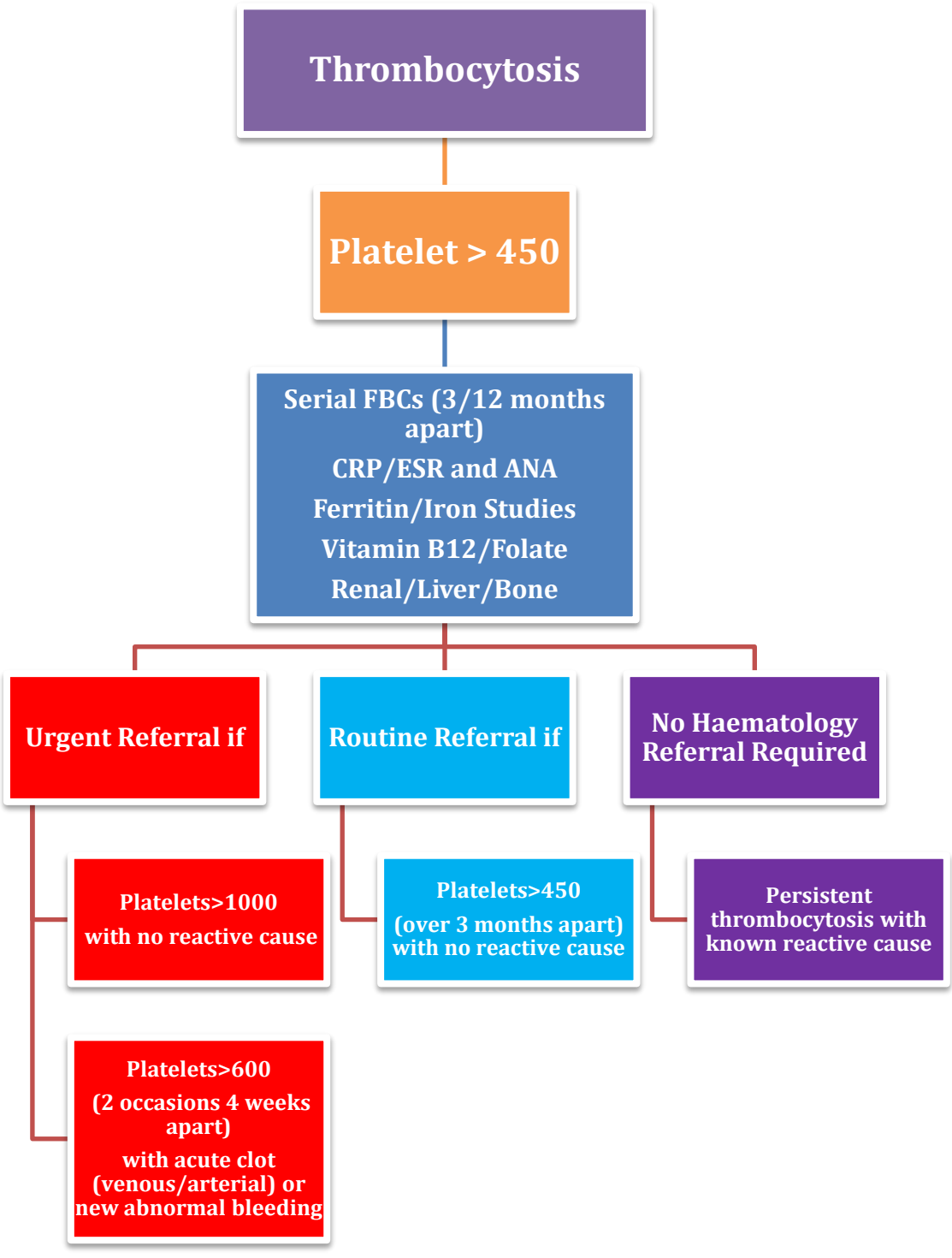
- Persistent thrombocytosis >1000 with no reactive cause
- Persistent thrombocytosis >600 (at least 2 occasions 4 weeks apart) in patients with acute thrombotic event (venous or arterial) or abnormal bleeding

Criteria for ROUTINE referral:

- Persistent thrombocytosis >450 (over 3 months apart) with no reactive cause

Who does not need referral to Haematology:

- Persistent thrombocytosis with known reactive cause.


Thrombocytosis
Platelet > 450
Serial FBCs (3/12 months apart)
CRP/ESR and ANA
Ferritin/Iron Studies
Vitamin B12/Folate
Renal/Liver/Bone
Urgent Referral if
Routine Referral if
No Haematology Referral Required
Platelets>1000
with no reactive cause
Platelets>450
(over 3 months apart)
with no reactive cause
Persistent thrombocytosis with known reactive cause
Platelets>600
(2 occasions 4 weeks apart)
with acute clot (venous/arterial) or new abnormal bleeding

10. Thrombocytopenia

Defined as platelet count **<150x 10/L:**

Most common causes of thrombocytopenia are infection, medications or normal variation. Other causes include peripheral destruction from immune thrombocytopenia purpura (ITP), bone marrow failure, alcohol, hypersplenism, disseminated intravascular coagulation (DIC) and Thrombotic microangiopathy (TTP/HUS)

Suggested Tests in Primary care:

- Assess for bleeding/bruising
- Review all medications
- Examine for lymphadenopathy and splenomegaly
- Blood film (exclude platelet clumping artefact)
- Vitamin B12/Folate/Ferritin/Iron studies
- HIV/Hep B and C serology
- Renal/Liver and bone bloods
- ANA

Criteria for IMMEDIATE referral (hospital admission):

- Platelet count <50 x 10^9/L and bleeding

Criteria for URGENT referral (out-patient assessment):

- Platelet count < 50 x 10^9/L, not bleeding and no known cause
- Platelet count 50-100 x 10^9/L
  -Accompanying cytopenia (Hb <10 g/dL and Neutrophils <1 x 10^9/L)
  -Splenomegaly or lymphadenopathy
  -Pregnancy
  -Planned surgery

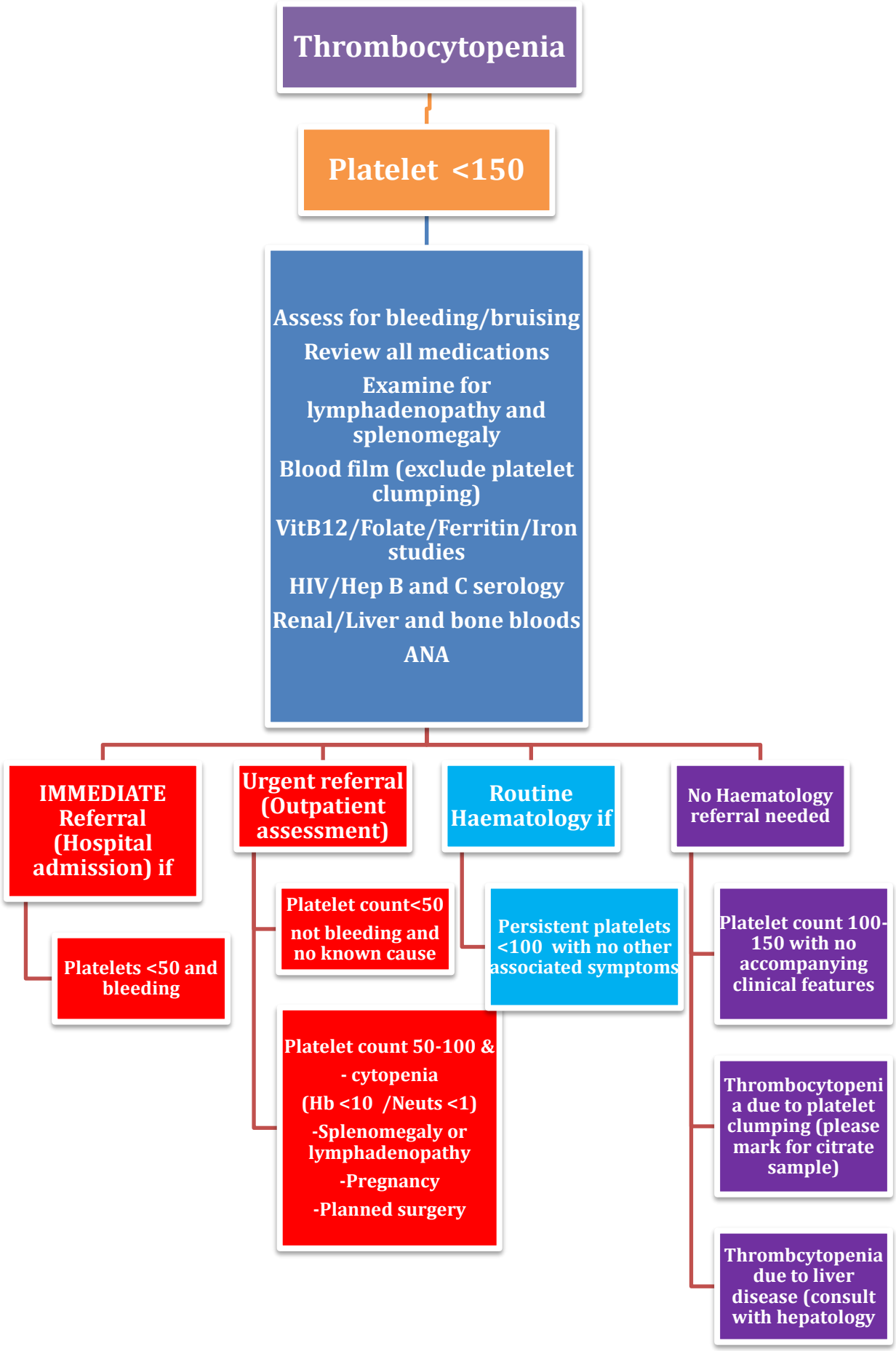
Criteria for ROUTINE referral:

- Persistent platelets count < 100 x 10^9/L (2 occasions 8 weeks apart) with no other associated symptoms

Who DOES NOT need referral to Haematology:

- Isolated platelet count 100-150 x 10^9/L with no accompanying clinical features
- If platelets are >100 x 10^9/L, repeat at 6 months and if remains >100 x 10^9/L, no requirement for ongoing monitoring
- Thrombocytopenia due to liver disease (consult with hepatology)
- Thrombocytopenia due to platelet clumping* (please mark for Thromboexact tube on blood form)

*some patients are prone to platelet clumping. This has no clinical consequence other than preventing an accurate platelet coujt. This problem can be circumvented by sending a request for a platelet count in a thromboexact tube.


Thrombocytopenia
Platelet <150
Assess for bleeding/bruising
Review all medications
Examine for lymphadenopathy and splenomegaly
Blood film (exclude platelet clumping)
VitB12/Folate/Ferritin/Iron studies
HIV/Hep B and C serology
Renal/Liver and bone bloods
ANA
IMMEDIATE Referral (Hospital admission) if
Platelets <50 and bleeding
Urgent referral (Outpatient assessment)
Platelet count<50 not bleeding and no known cause
Platelet count 50-100 & - cytopenia (Hb <10 /Neuts <1) -Splenomegaly or lymphadenopathy -Pregnancy -Planned surgery
Routine Haematology if
Persistent platelets <100 with no other associated symptoms
No Haematology referral needed
Platelet count 100-150 with no accompanying clinical features
Thrombocytopenia due to platelet clumping (please mark for citrate sample)
Thrombcytopenia due to liver disease (consult with hepatology

11. Polycythaemia

Relative polycythaemia is due to reduced plasma volume associated with diuretics, dehydration or alcohol.

Absolute polycythaemia refers to increase in red cell mass. Secondary causes of absolute polycythaemia are more common than primary causes such as polycythaemia vera (PV).
The most common secondary cause is hypoxia (smoking, chronic lung disease or congenital heart disease) or testosterone/anabolic steroid use.
JAK2V617F mutation is present in 97% of patients with PV.

Suggested tests in primary care:

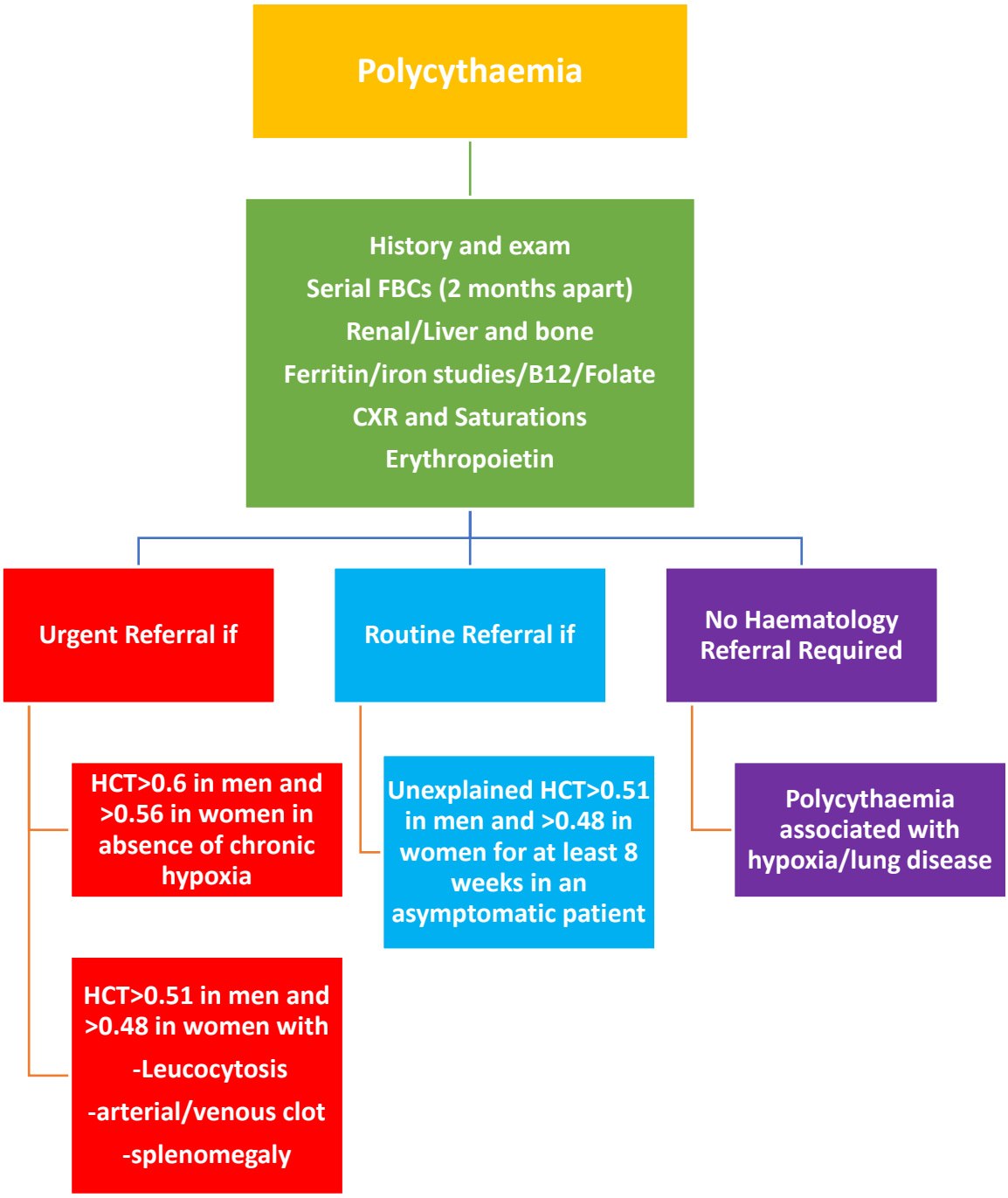
- History and exam (clue to secondary causes)
- Serial FBCs at least 2 months apart
- Renal/Liver and bone bloods
- Ferritin/ iron studies/Vit B12/Folate
- CXR and Sats
- Erythropoietin (expected to be low or subnormal)

Criteria for URGENT referral:

- Haematocrit >0.6 in men and >0.56 in women in absence of chronic hypoxia
- Haematocrit >0.51 in men and >0.48 in women associated with
    - Leucocytosis
    - arterial/venous clot
    - splenomegaly

Criteria for ROUTINE referral:
Persistently raised unexplained haematocrit >0.51 in men and >0.48 in women for at least 8 weeks in an asymptomatic patient

Who does not need referral to Haematology:
Polycythaemia associated with hypoxia/lung disease or testosterone use. Consider referral to cardiology or respiratory


Polycythaemia
History and exam
Serial FBCs (2 months apart)
Renal/Liver and bone
Ferritin/iron studies/B12/Folate
CXR and Saturations
Erythropoietin
Urgent Referral if
Routine Referral if
No Haematology Referral Required
HCT>0.6 in men and >0.56 in women in absence of chronic hypoxia
HCT>0.51 in men and >0.48 in women with
-Leucocytosis
-arterial/venous clot
-splenomegaly
Unexplained HCT>0.51 in men and >0.48 in women for at least 8 weeks in an asymptomatic patient
Polycythaemia associated with hypoxia/lung disease

12. Raised Vitamin B12

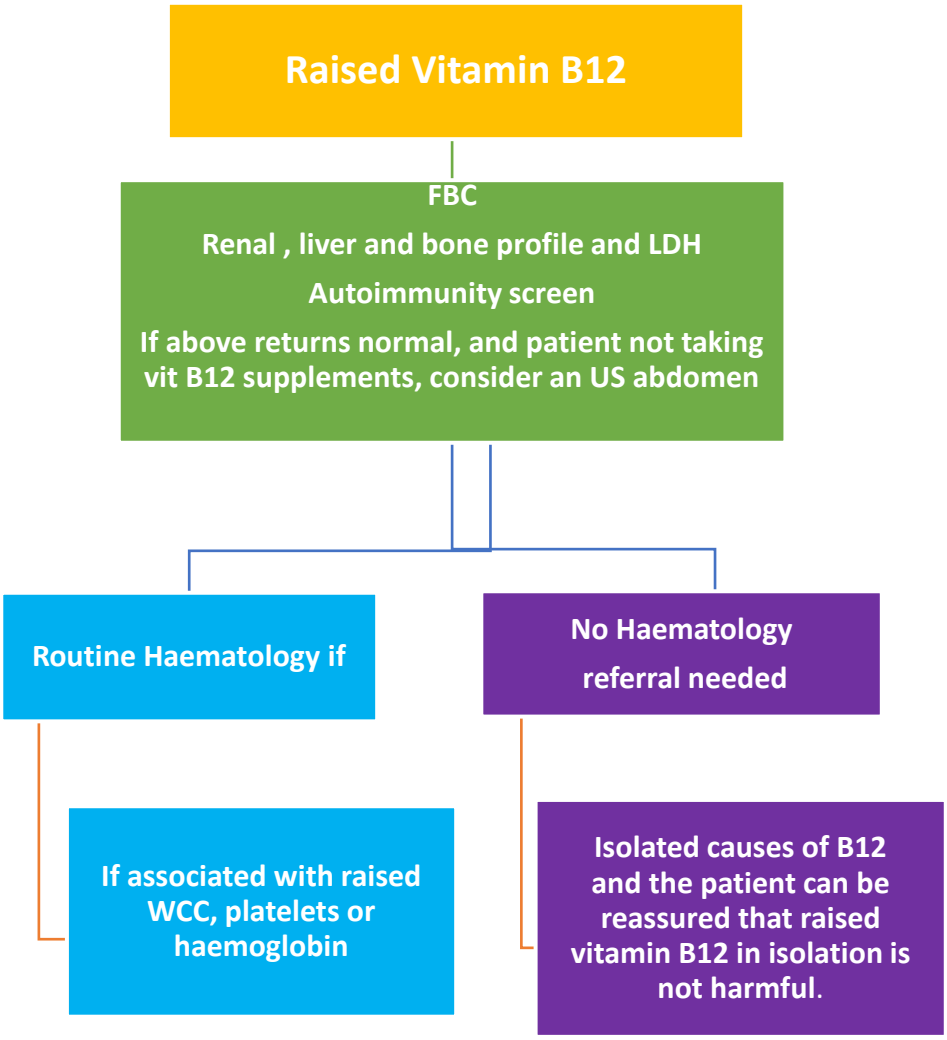
The most common cause of raised Vitamin B12 are liver or renal disease, myeloproliferative neoplasms and autoimmunity.
Review medications including multivitamins or foods that have high vitamin B12 content.

Suggested tests in Primary care:

- FBC
- Renal, liver and bone profile and LDH
- Autoimmunity screen
- If above returns normal, and patient not taking vitamin B12 supplements, consider an US abdomen

Criteria for ROUTINE referral:
If associated with raised WCC, platelets or haemoglobin

Who does not need referral to Haematology:
Isolated causes of elevated B12 and the patient can be reassured that raised vitamin B12 in isolation is not harmful.



13. Lymphadenopathy

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

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

Suspicions for lymphoma should be increased in the presence of generalised / progressive lymphadenopathy, hepatosplenomegaly or B related symptoms (Drenching night sweats, unexplained fevers, and > 10% weight loss in six months).

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

Suggested tests in primary care:

- FBC
- Blood film
- ESR and CRP
- U+E, LFTs, LDH, Bone Profile
- Viral serology for EBV / HIV / hepatitis B and C
- CXR
- referral for ultrasound of nodes – this can be useful for determining whether they are reactive or suspicious
- **Refer to appropriate specialty for node biopsy***

*Haematology does not offer a biopsy service for tissue diagnosis and therefore ***concurrent*** *referral to an appropriate specialty* for excision biopsy will help speed up the diagnostic process and should occur in the first instance, e.g.:

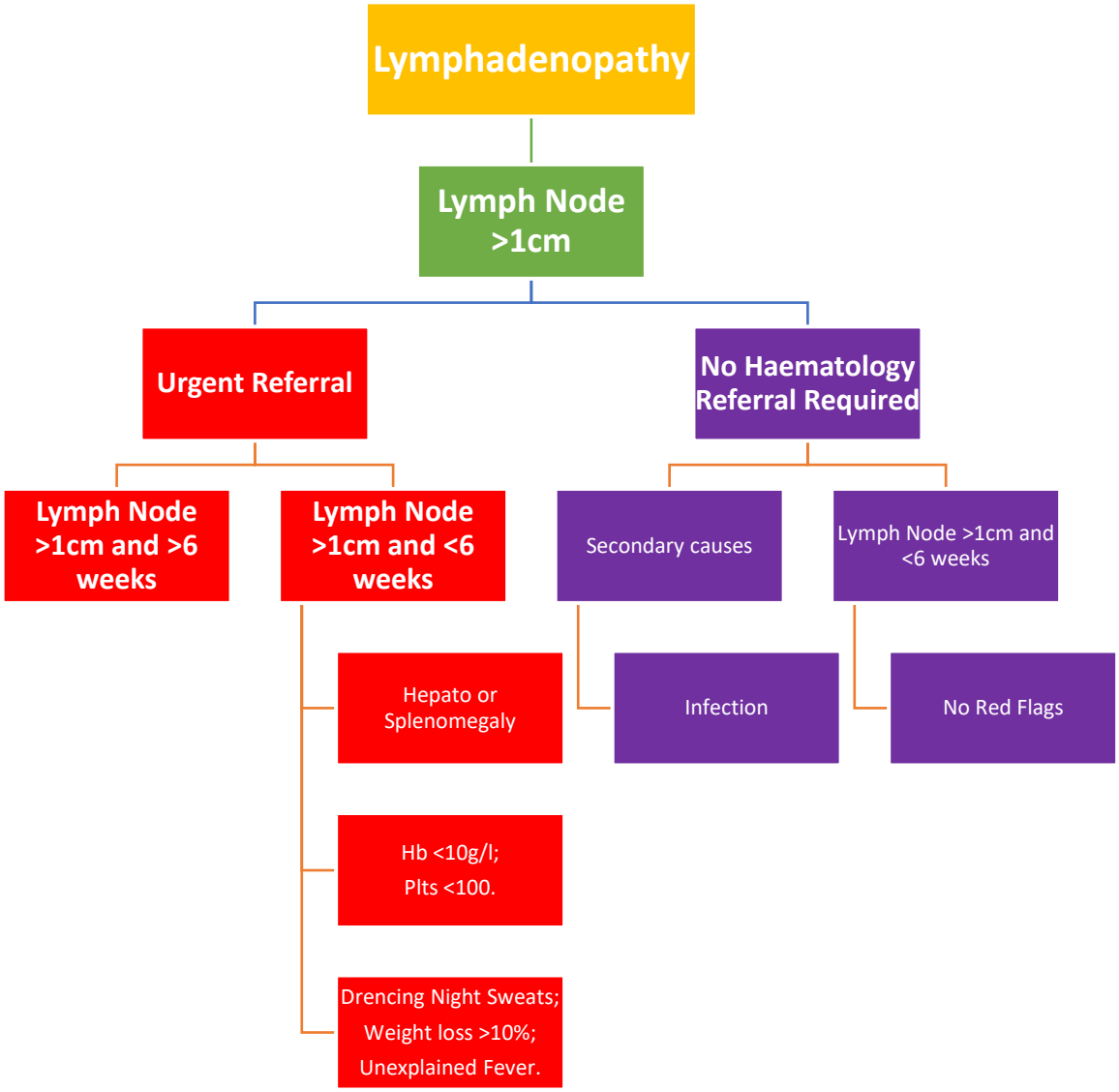
- Neck nodes directed to ENT
- Axillary nodes directed to Breast & General Surgery
- Inguinal nodes directed to general surgery

Bone marrow examination should be reserved for staging in confirmed lymphoma or leukaemia cases – it is not a useful primary investigation of lymphadenopathy as a normal exam does not exclude the presence of lymphoma.

Criteria for URGENT referral:

- Lymphadenopathy >1cm present for >6 weeks with no infective precipitant
- Lymphadenopathy of >1cm and <6 weeks in association with
    - B Symptoms (See above)

- Hepatomegaly or Splenomegaly
- Rapid nodal enlargement
- Disseminated / Generalised nodal enlargement
- Anaemia, Thrombocytopenia or Leucopenia
- Hypercalcaemia



14. Sweats

Patients with 'sweats' are often referred to haematology for investigation of possible haematological malignancy. This is a common non-specific symptom and the majority of patients do not have a haematological malignancy.

Although haematological malignancy can cause drenching night sweats (Drenching night sweats that soak bed clothes or bedding), it is unusual for this to be the sole presenting feature.

Other systemic features include unexplained weight loss (>10% body weight within 6 months), lymphadenopathy / splenomegaly or an abnormal full blood count.

Infection	Acute or chronic infections including tuberculosis, endocarditis and HIV infection
Endocrine	Menopause, hyperthyroid, diabetes mellitus, phaeochromocytoma, carcinoid syndrome or acromegaly.
Neurological	Parkinsonism or autonomic neuropathy
Malignancy	Haematological malignancy including myeloproliferative disorders or lymphoma
Medication	Antidepressants (SSRIs, especially venlafaxine, and tricyclics), hormonal agents (e.g. tamoxifen, GnRH agonists) or NSAIDs.
Withdrawal Effect	Alcohol Other illicit substances
Other	Obstructive Sleep Apnoea Connective Tissue Diseases

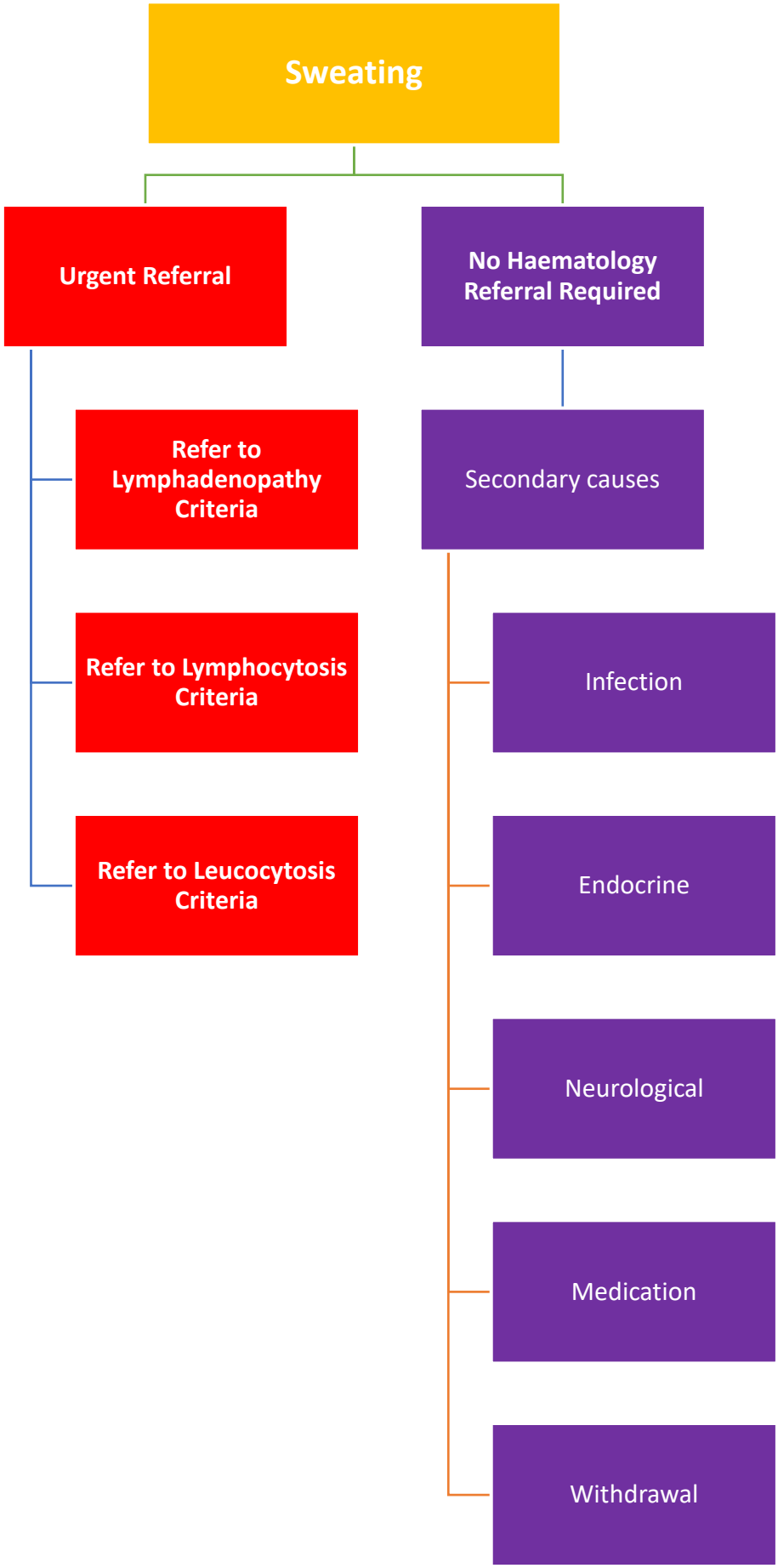
Suggested tests in primary care (Dependent on clinical presentation):

- Clinical examination for lymph nodes &/or splenomegaly
- FBC
- Blood film
- LDH, ESR and CRP
- TFTs
- Glucose
- Viral serology for EBV / CMV / HIV / Hepatitis B and C
- Immunoglobulins
- Gonadotrophins
- CXR

Criteria for referral:

- Significant additional systemic symptoms such as unexplained weight loss / fever / alcohol induced pain
- Associated lymphadenopathy and / or splenomegaly
- Abnormal FBC

Please discuss with haematologist to see if possibly related and therefore, referral warranted


Sweating
Urgent Referral
No Haematology Referral Required
Refer to Lymphadenopathy Criteria
Refer to Lymphocytosis Criteria
Refer to Leucocytosis Criteria
Secondary causes
Infection
Endocrine
Neurological
Medication
Withdrawal

15. Splenomegaly

Palpable spleen or an enlarged spleen detected by imaging. Spleen of >13cm is usually considered enlarged. However, spleen size increases with height. On average spleen length increases by 0.2cm for every 1inch over 6 foot.

Whilst haematological disorders are associated with splenomegaly, there are numerous non-haematological causes that need to be considered.

Infections	Viral
	Bacterial
	Parasitic
Systemic Disorders	Chronic Liver Disease
	Connective Tissue Disease
	Gaucher's
	Sarcoidosis
	Cardiac Failure
	Alcohol
Haematological	Auto-Immune Haemolytic Anaemia
	Hereditary Spherocytosis
	Myeloproliferative Disorders
	Myelofibrosis
	Leukaemia
	Lymphoproliferative disorders

Suggested tests in primary care:

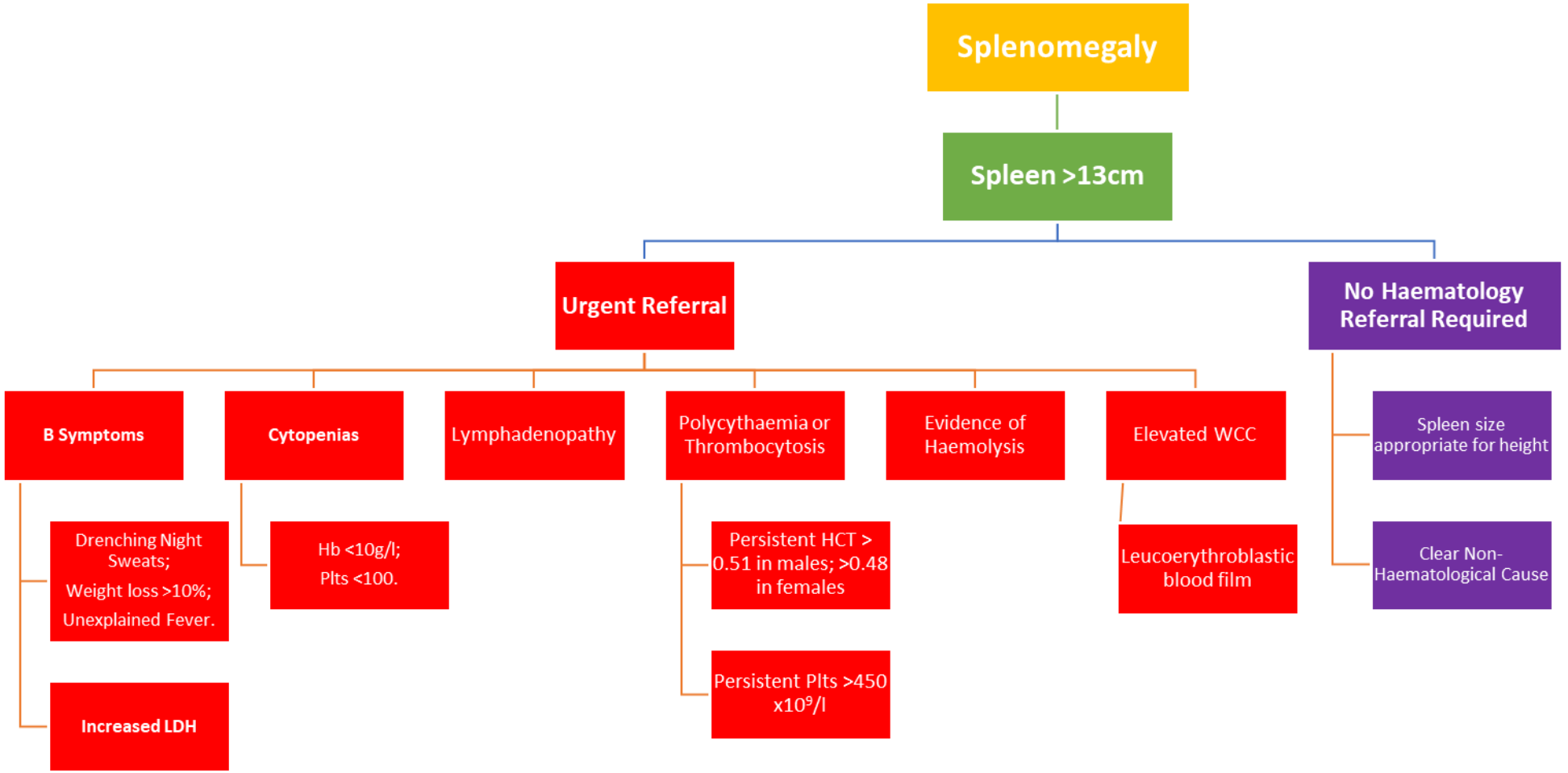
- FBC
- Blood film
- ESR and CRP
- Reticulocyte count. If increased check a direct antiglobulin test (DAT)
- LFTs, GGT, AST, LDH
- Viral serology for EBV / HIV and hepatitis viruses
- Immunoglobulins + serum electrophoresis

Criteria for urgent referral:

- Significant systemic symptoms such as unexplained weight loss (> 10% in six months), drenching sweats or unexplained persistent fever
- Lymphadenopathy
- Evidence of haemolysis (raised reticulocyte count, LDH, bilirubin)
- Abnormal FBC (cytopenias, lymphocytosis or leucoerythroblastic film)

Who does not need referral to Haematology:

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


Splenomegaly
Spleen >13cm
Urgent Referral
No Haematology Referral Required
B Symptoms
Cytopenias
Lymphadenopathy
Polycythaemia or Thrombocytosis
Evidence of Haemolysis
Elevated WCC
Drenching Night Sweats;
Weight loss >10%;
Unexplained Fever.
Increased LDH
Hb <10g/l;
Plts <100.
Persistent HCT > 0.51 in males; >0.48 in females
Persistent Plts >450 x10^9/l
Leucoerythroblastic blood film
Spleen size appropriate for height
Clear Non-Haematological Cause

16. Paraproteinemia

These are disorders characterised by the production of a paraprotein and include monoclonal gammopathy of undetermined significance (MGUS), multiple myeloma and Waldenström macroglobulinaemia. Paraproteins may also be a feature of CLL, non-hodgkin lymphoma, or AL amyloidosis.
The prevelance of MGUS increases with age. 6.2% over 60s and 10% over 80s The overall risk of MGUS progression to myeloma is around 1% per year and this remains static.

Referrals to haematology **should not** be made for patients with raised immunoglobulin levels / gamma globulin levels in the absence of a immunofixable monoclonal paraprotein band on serum electrophoresis. Polyclonal gammopathy implies a non-specific immune reaction.
Serum free light chains can be elevated in different situations especially in renal failure. Refer if either Kappa or Lambda light chains over 200 or if Kappa/Lambda ratio is abnormal.

Criteria for URGENT referral:
Any new paraprotein with accompanying features suggestive of multiple myeloma or other haematological malignancy.

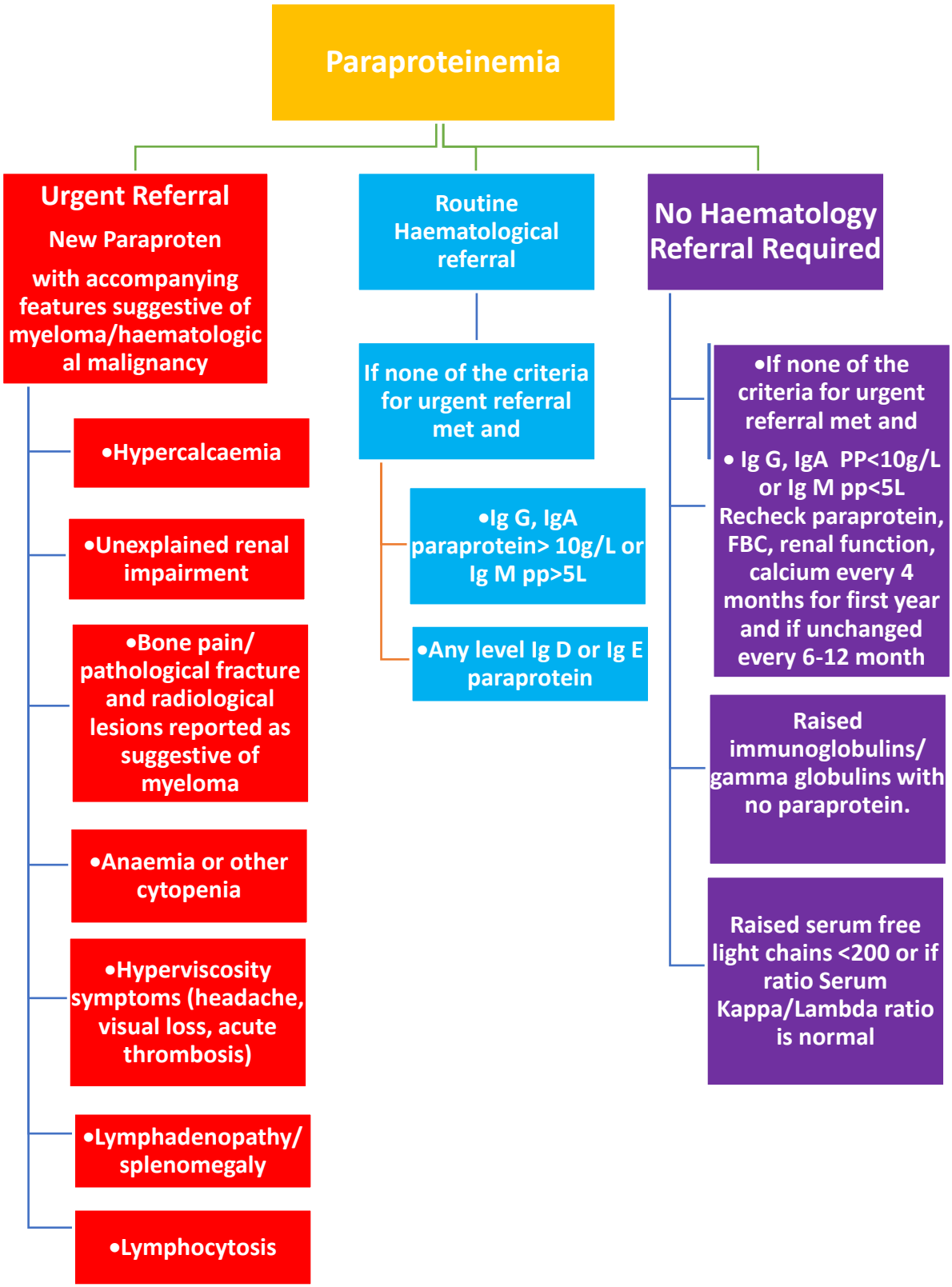
- Hypercalcaemia
- Unexplained renal impairment
- Bone pain or pathological fracture and radiological lesions reported as suggestive of myeloma
- Anaemia or other cytopenia
- Hyperviscosity symptoms (headache, visual loss, acute thrombosis)
- Lymphadenopathy or splenomegaly
- Lymphocytosis

Criteria for ROUTINE referral:
If none of the criteria for urgent referral met and

- Ig G, IgA paraprotein> 10g/L or Ig M pp> 5g/L
- Any level Ig D or Ig E paraprotein

Who does not need referral to Haematology:
If none of the urgent criteria met and Ig G, IgA paraprotein<10g/L or Ig M pp < 5g/L

- Recheck paraprotein, FBC, renal function, calcium every 4 months for first year and if unchanged every 6-12 month
- If band has increased by >25%, (a minimum of 5g/L) – send for routine referral


Paraproteinemia
Urgent Referral
New Paraproten
with accompanying features suggestive of myeloma/haematological malignancy
•Hypercalcaemia
•Unexplained renal impairment
•Bone pain/ pathological fracture and radiological lesions reported as suggestive of myeloma
•Anaemia or other cytopenia
•Hyperviscosity symptoms (headache, visual loss, acute thrombosis)
•Lymphadenopathy/ splenomegaly
•Lymphocytosis
Routine Haematological referral
If none of the criteria for urgent referral met and
•Ig G, IgA paraprotein> 10g/L or Ig M pp>5L
•Any level Ig D or Ig E paraprotein
No Haematology Referral Required
•If none of the criteria for urgent referral met and
• Ig G, IgA PP<10g/L or Ig M pp<5L
Recheck paraprotein, FBC, renal function, calcium every 4 months for first year and if unchanged every 6-12 month
Raised immunoglobulins/ gamma globulins with no paraprotein.
Raised serum free light chains <200 or if ratio Serum Kappa/Lambda ratio is normal

17. Venous Thromboembolic Events

Risk Factors/Provoking events for VTE	
Surgical	• Hip and knee surgery • Other surgeries
Non-surgical Transient	• Immobility/bed ridden>3 days • Hospitalisation • Trauma • HRT/Oestrogen contraceptive pill (highest risk in 1st year) • Pregnancy/Post-natal
Non-surgical Permanent	• Cancer • Antiphospholipid syndrome

Initial assessment in Emergency Department:

- Once a diagnosis of VTE has been established, patient should continue on anticoagulation for at least 3 months.
- Patients should have a detailed clinical assessment including a systemic review and clinical examination to assess for red flags that may warrant further investigation
- Ensure patient is adherent with anticoagulation and there are no bleeding complications
- Routine thrombophilia is NOT recommended

Criteria for ROUTINE referral:

- DVT/PE is unprovoked or associated with transient risk factor
- Recurrent VTE
- VTE provoked by cancer or antiphospholipid syndrome
- VTE at unusual site
- Where the length of anticoagulation beyond 3 months is not clear, please discuss with the registrar covering coagulation in SVUH and/or refer to local haematology.

Who does not need referral to Haematology:

Patients with proven PROVOKED VTE

- All patients with proven VTE should receive anticoagulation for a minimum of 3 months
- Patients with DVT/PE provoked by hip/knee surgery or major trauma can stop anticoagulation after 3 months as long as the provoking factor has resolved
- Recurrent VTE generally require ongoing anticoagulation

18. Abnormal Coagulation Results

Common causes	
Isolated prolonged APTT	• Heparin • Lupus anticoagulant • Deficiency in Factor VIII, IX, XI & XII
Isolated prolonged PT	• Deficiency in Factor VII
Prolonged PT/APTT	• Vitamin K Deficiency • Liver disease • Warfarin treatment • Factor Xa inhibitors (Rivaroxaban/Apixiban) • Direct thrombin inhibitors (Dabigatran) • DIC

Suggested tests in Primary Care:

- Repeat coagulation sample and review any historical results
- Assess clinical for any bleeding disorder (previous surgeries/dental extraction/prior pregnancies etc.)
- Assess for underlying liver abnormality
- Review drug history especially anticoagulant

Criteria for ROUTINE referral:

- Abnormal coagulation screen with personal bleeding history
- Abnormal coagulation screen with a family history of inherited bleeding disorder
- Persistent abnormal coagulation screen without an obvious cause

Who does not need referral to Haematology:

- Abnormal coagulation screen on anticoagulant
- Abnormal coagulation with established liver disease

19. Easy Bruising/Bleeding

Common referral and very rarely find underlying haematological cause.

Common causes include senile purpura secondary to collagen loss and actinic damage
Other causes include

- drug related bruising/bleeding (anticoagulants and steroids)
- a manifestation of a vascular defect (renal failure, collagen disease)
- trauma or non-accidental injury
- inherited bleeding disorder

Suggested workup in Primary Care:

Bleeding History

- review to assess frequency, severity, pattern and anatomical site of bruises or bleeding
- Bleeding from an early age make hereditary disorder more likely
- Concerning features include bleeding without trauma, bleeding at multiple sites and excessive bleeding post-surgical or dental procedure
- ISTH bleeding assessment tool is an excellent screening tool ISTH-SSC Bleeding Assessment Tool (certe.nl)

Drug History

- Anticoagulants and antiplatelets especially if used in combination
- Steroid use

Family History

- Presence of a family member with similar bleeding symptoms raises possibility of an inherited bleeding disorder

Co-morbidities

- Certain conditions such as renal or liver dysfunction can be associated with increased risk of bleeding/bruising

FBC, renal and liver profiles
Coagulation screen (PT and APTT) +/- Fibrinogen level

Criteria for ROUTINE referral:

- Large or multiple bruises in unusual sites without an obvious cause
- Severe and/or prolong bleeding without an obvious cause
- Prolonged and excessive bleeding post procedure or surgery
- If Family history of inherited bleeding disorder, please refer to National Coagulation centre in St James' Hospital