HAEMATOLOGY

National Referral Guidelines

SPECIFIC HAEMATOLOGY REFERRAL LETTER GUIDELINES
Referrals can be accepted from registered Medical and Dental Practitioners and midwives.

NATIONAL REFERRAL GUIDELINES : HAEMATOLOGY			
Diagnosis	**Evaluation**	**Management Options**	**Referral Guidelines**
Haematology can be categorised into the following categories: • Bleeding disorders • Thrombotic disorders • Anaemia • Acute Malignant Disorders • Chronic Malignant Disorders • Miscellaneous	A thorough history and physical examination is required to determine the specific diagnosis (see below). Full blood count is mandatory for all Haematological referrals. **Please ensure copies of all investigations are sent/faxed with referral.**	Specific treatments depend on the specific diagnoses identified, as noted.	Circumstances for referral are indicated below with reference to the appropriate speciality/ specialities.

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National Referral Guidelines

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Diagnosis	**Evaluation**	**Management Options**	**Referral Guidelines**
BLEEDING DISORDERS			
Familial Conditions	**Key Points:** • Detailed family history • Detailed type of bleeding e.g. mucocutaneous or joint bleeding • Investigations: • Initial/basic coagulation screen (platelet count, IR/INR, APTT, fibrinogen, bleeding time). For more detailed investigations discuss with haematology laboratory.	If acutely bleeding consult with haematology service.	• Acute bleeding should be referred for admission - category 1. • Pre-surgery assessment - refer category 1-2. Needs to include date of proposed surgery.* • Carrier status assessment - category 3 with the exception of pregnant women – category 2. * depends on urgency of procedure
Bleeding disorders of uncertain cause	Key points: • May have a family history. • Type of bleeding, e.g. mucocutaneous or joint bleeding. • Drug history • Post-surgical bleeding? • Post-trauma bleeding? • Investigations: • Initial coagulation screen • CBC • LFTs • Renal function	Consider stopping NSAID and aspirin. If acutely bleeding consult with haematology service.	• Acute bleeding should be referred for admission – category 1. • Pre-surgery assessment - refer category 1-3 depending on urgency of surgery • Carrier status assessment - category 3. • Unless pregnant – then category 2.
Thrombocytopenia	**Key points:** • Duration • Detailed past history, e.g liver disease, autoimmune • Drug history • Alcohol history • Investigations: • CBC and ESR • LFTs • Renal function • MSU • ANF/autoimmune screen	Discontinue NSAID and aspirin unless clear indication to continue. Review drug history and stop offending agents if possible.	• Patients with a count less than 20 x 10^9/L should be referred for admission or same day O.P. assessment - category 1. • Patients with a count less than 50 x 10^9/L refer for urgent outpatient assessment – category 2. • Stable/mild thrombocytopenia less than 100 x 109/ L refer for outpatient assessment - category 3. May not be required unless other abnormalities in counts, or other reasons – eg. surgery needed splenomegaly, pregnancy.

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Diagnosis	**Evaluation**	**Management Options**	**Referral Guidelines**
THROMBOTIC DISORDERS			
Familial Thrombotic Disorders	**Key points**: • Detailed family history • Detailed type of thrombosis e.g. venous or arterial. • Recurrent or single event? • Recent surgery/trauma • Pregnancy • Drug history Investigations: • Coagulation screen • If familial defect known, appropriate factor assay only. • Appropriate full thrombophilia workup only after discussion with Haematologist.	Anticoagulation therapy should be continued as previously recommended until Haematology review. If pregnant will require a joint approach between Haematologist / Specialist Physician and Specialist Obstetrician.	• Acute thrombotic event requires urgent assessment query admission to acute medical team - category 1. • Assessment required prior to planned surgery or pregnancy - category 2-3 depending on timing. *Note : some centres have a thrombosis clinic / service for outpatient thrombosis treatment measures*
Thrombotic disorders of uncertain cause	**Key points:** • May have a family history. • Type of thrombosis, e.g.DVT, arterial thrombosis • Drug history including oral contraceptive or HRT. • Post-surgical thrombosis? • Post-trauma thrombosis? • Pregnancy associated thrombosis? • Important group aged under 40 recurrent unexplained thrombosis. Investigations: • Coagulation screen • CBC/ESR • LFTs • Renal function • Appropriate full thrombophilia workup Suggest discuss with Haematologist.	Anticoagulation therapy should be continued as previously recommended until Haematology review. If pregnant will require a joint approach between Haematologist / Specialist Physician and Specialist Obstetrician.	• Acute thrombotic event requires urgent assessment query admission to acute medical team - category 1. • Assessment required prior to planned surgery or pregnancy - category 2-3 depending on timing. • May need to be referred after completing course anticoagulant therapy to assess thrombophilia risk

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Diagnosis	Evaluation	Management Options	Referral Guidelines
ANAEMIA	**Key points:** • Duration of anaemia. • Previous anaemia assessment. • Family history • Bleeding history especially menstrual loss • Dietary history • Drug history • Exclude surgical causes of iron deficiency Investigations: • CBC/ESR/CRP • B12/red cell folate • Iron studies including ferritin • Reticulocytes • Renal function • LFTs • Immunoglobulins and serum protein electrophoresis • MSU • Haptoglobins • Faecal occult bloods	Uncomplicated iron / folate / B12 deficiency to be managed by primary carer. Most iron deficiency/anaemia does not require Specialist Haematological assessment. Referral should be considered if patients shows sub optimal response to replacement therapy after deficiency state confirmed Referral to other specialists service may be required for investigation/managing the cause of iron/B12 or folate deficiency.	• Persistent unexplained anaemia - category 2 or 3. • Haemolytic anaemia of any cause - category 1 or 2. • Evidence of a leukoerythroblastic blood picture or pancytopenia requires a more urgent referral.
ACUTE MALIGNANT DISORDERS			
Acute leukaemia / highgrade lymphoma	**Key points:** Any suspicion of acute leukaemia/ highgrade lymphoma requires urgent discussion with Haematologist. For example: 1. Liver, renal functions, calcium, CBC or marrow examination suggesting acute leukaemia / lymphoma. 2. High index or suggestive clinical signs, e.g. bleeding gums, splenomegaly, PUO lymphadenopathy Investigations: • CBC • LFT's, creatinine • Calcium	Ring Haematologist on call.	Acute leukaemia - immediate referral with a view to admission - category 1. LYMPHOMAS - Fax urgent referral. Depending on severity of symptoms may require urgent admission / O.P. appointment or be seen semi-urgently.

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CHRONIC MALIGNANT DISORDERS			
Chronic Myeloid Leukaemia	Key points • May present with splenomegaly • Frequently detected following routine CBC with high white cell count	• Patients with very high white cell counts (>100 x 10^9/l) and/or massive splenomegaly. Discuss with Haematologist urgently. • Less advanced cases can be seen urgently in outpatient clinics.	Ring Haematologist on call with a view to immediate admission – category 1. • Refer to urgent outpatient clinic - category 1.
Chronic Lymphocytic Leukaemia	**Key points:** • Many cases are early disease with normal haemoglobin and platelets and no splenomegaly. • If Hb and platelet count normal – refer film to haematologist. • Do surface markers to confirm disease if lymphocyte count >5x10^9 >3 months or if >20X10^9 on the first count.		• Referral category 3. • Progressive disease with anaemia, lymphadenopathy, splenomegaly and thrombocytopenia require referral urgent - category 2. • Complications of haemolysis requires immediate referral - category 1. • Complications of infection –cateory 1-2
Myelodysplastic disorders	**Key Points:** • This is a spectrum of disorders presenting with unexplained cytopenias of varying severity. • A bone marrow examination is recommended.	Patients with active infection and/or ongoing bleeding discuss with Haematologist.	• Acutely unwell patients secondary to neutropenia or thrombocytopenia require immediate admission - category 1. • Uncomplicated patients outpatient referral category 2 - 3.
Myeloproliferative Disorders Incuding polycthaemia +/- raised WBC's, +/- thrombocytosis of unexplained cause	**Key points:** • As above, this is a spectrum of disorders presenting with unexplained raised haemoglobin, platelets and neutrophils.		• Patients with clinical hyperviscosity, thrombosis or bleeding for admission - category 1 • Uncomplicated refer to outpatient assessment - category 2 or 3.

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Diagnosis	**Evaluation**	**Management Options**	**Referral Guidelines**
Myeloma/Plasmacytoma and related disorders	**Key points:** • Bone pain • Anaemia • Hypercalcaemia • Cord compression • Renal failure • Hyperviscosity • Infection Investigations: • CBC/ESR • Reticulocytes • Renal function • LFTs • Calcium • Immunoglobulins and electrophoresis • MSU/Bence-Jones protein • Bone marrow • X-ray of painful areas		• Acutely unwell patients secondary to hypercalcaemia, cord compression, renal failure or hyperviscosity require immediate admission - category 1. • Uncomplicated patients outpatient referral category 1. • Asymptomatic Category 3. Low level paraproteins e.g. IgG < 20 with absent BJP ; IgA <5[1].
Marrow Hypoplasia/Aplasia	**Key points:** • Many chronic or inherited haematological conditions will have been identified by laboratory testing. • Consider drug induced causes.	(An urgent bone marrow may be required - discuss with Haematologist.)	• Most of these referrals are outpatients -category 2. • Referral is appropriate for the following conditions: • Hereditary haemolytic anaemias • Chronic neutropenia • Unexplained chronic eosinophilia • Hypogammaglobulinaemia • Severe cytopenia, platelets < 30, neutrophils < 1 - contact Haematologist.[category 1]
Pancytopenia (without cause obvious on blood film)	Investigations • Check red cell folate, in otherwise B12/RC folate • Check spleen size • LFT's • Reticulocytes	• Stop drugs which may be causing aplasia • Bone marrow may be required Possible Diagnosis would include: • Aplastic anaemia • Marrow infiltration • Other bone marrow • Megablastic anaemias • Hyposplenism	• Severe cytopenia platelets < 30, neutrophils <1 – phone Haematologist.[category 1] • Other patients with this diagnosis – refer to Outpatients – usually category 2, depending on full blood count results.

[1]Low level paraproteins in asymptomatic patients may not require referral but the paraprotien should be monitored at 3-6 monthly intervals. In rare cases a paraproetin may be associated with lymphoma or amyloidosis.

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Isolated Neutropenia	**Key points:** • Consider drug effect • If persistent autoantibody screen e.g. ANF	• ANC <0.5 and febrile • ANC <0.5 and unexplained (confirm) • If mild , ANC 1.0 – 2.0 may be 2º to viral infection – repeat 4-8 weeks, if persistent may require referral • Will depend on coexisting problems (including impending surgery) or symptoms • Discontinue any possible drugs	• Refer category 1 • Refer category 2-3. • Refer category 2-3
Postsplenectomy Advice		• Vaccination/advice may be carried out by GP. Repeated 2-5 yearly (depending on type). At present vaccinations not subsidised.	• Referral for advice – category 3.
Other conditions eg: • Unexplained chronic eosinophilia • Hypogammaglobulinaemia			• Refer Outpatients. • Urgency depends on blood results.
Hereditary Haemochromatosis	**Key points:** • Often asymptomatic - detected on family screening or "routine" blood tests • May have personal or family history of cirrhosis, diabetes, arthritis, heart failure, hypogonadism Investigations: • Fasting transferrin (TIBC) saturation • Ferritin • HFE Gene analysis • Liver enzymes • Glucose	Liver biopsy is generally unnecessary for diagnosis but may be indicated in some circumstances.	• Confirmed diagnosis of hereditary haemochromatosis or diagnostically difficult cases without evidence of significant end organ - outpatient referral category 3-4 • Confirmed diagnosis of hereditary haemochromatosis with evidence of end organ damage (e.g.abnormal liver enzymes, diabetes, heart failure, hypogonadism) – outpatient referral category 2-3
Porphyria cutanea tarda for venesection		Referral maybe indicated for venesectionprogramme	Category 3
Monoclonal Gammopathies of Underminer Significance (MGUS)	1gG paraprotein level of < 20g/L with no other suspicious features eg weight loss, night sweats, malaise, lymph node swellings, infections or back pain. GP follow up. 1gG paraprotein > 20g/L, any other suspicious clinical laboratory features and patients under 60 years of age.	See appendix 1	Asymptomatic cat 4 Refer if evidence of disease progression (eg 1gG paraprotein > 20)

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Monoclonal Gammopathies of Undetermined Significance

APPENDIX 1

Department of Haematology, Christchurch Hospital - February 2000

The monoclonal gammopathies are a group of disorders characterised by proliferation of a single clone of plasma cells or lymphoid cells that produce homogeneous monoclonal (M) protein. This paraprotein is usually detected by serum protein electrophoresis (SPE). The paraprotein is most often IgG. Disorders characterised by production of paraprotein include monoclonal gammopathy of undetermined significance (MGUS - also called benign monoclonal gammopathy), multiple myeloma and Waldenstrom's macroglobulinaemia. Paraprotein may also be associated with quite a number of other conditions including amyloidosis, chronic lymphocytic leukaemia, and occasionally non-Hodgkin's lymphoma. The incidence of monoclonal gammopathy increases with age, being approximately 1% above 25 years, 3% above 70 years and up to 10% above 80 years of age. MGUS describes the presence of a monoclonal paraprotein of serum immunoglobulin in the absence of clinicopathological evidence of multiple myeloma or the other diseases mentioned above. Patients with MGUS are typically asymptomatic and the paraprotein is often an incidental finding. There are no abnormal physical findings and lack of progression on followup with demonstration of no other evidence of progressive plasma cell or B-cell lymphoproliferative malignancy are the basic diagnostic criteria for a diagnosis. The term MGUS is used in preference to benign monoclonal gammopathy, as one does not know which of these patients will evolve in time to having a significant disease.

In general terms, the lower the level of the monoclonal band, the less likely the patient is to have significant disease. However, this is not an absolute, and it is very important that appropriate questions in terms of symptomatology are asked, such as weight loss, night sweats, malaise, lymph node swellings, infections and bone pain, Likewise it is important to check for paraprotein in the urine and other basic blood parameters, such as full blood count, other immunoglobulin levels, Beta 2 microglobulin, and in particular, calcium, albumin and creatinine.

There is no precise level of serum M protein at which to predict those patients who will have MGUS rather than progressive disease. However, in the case of a patient with an IgG level paraprotein level of <20g/L (or an IgA paraprotein level <10g/L or IgM paraprotein level <10g/L), with no other suspicious features, **we would advocate GP followup with clinical review and blood tests, CBC, serum electrophoresis? BJP urine, calcium and creatinine at approximately 6 monthly intervals in patients older than 60. The features which specifically need to be documented are absence of bone pain, night sweats, weight loss, lymphadenopathy, hepatosplenomegaly, anaemia or other abnormalities on the full blood count, increased LD, hypocalcemia, renal impairment, the absence of Bence Jones Proteinuria or reduction of the other immunoglobulin levels.** With patients who have an IgG paraprotein level of >20 (or an IgA paraprotein 10g/L or an IgM paraprotein of >10 g/L), any other suspicious clinical (e.g. of amyloidosis), laboratory features and patients less than 60, an outpatient referral should be made to the Haematology or Oncology departments. A bone marrow examination in this situation may reveal a slightly increased number of plasma cells, which in itself is may not be diagnostic of myeloma, but may indicate that the patient needs to be reviewed somewhat more often, and further investigations such as skeletal survey and Beta 2 microglobulin performed. If, on the other hand, the plasma cell and lymphocyte count is normal the patient will probably be referred back to the GP for ongoing 6 monthly monitoring with guidelines as to when to re-refer.

In the large study from the Mayo clinic (Ref 1) 18% of patients had developed myeloma, amyloidosis or lymphoma at 10 years of followup. It is important to stress to patients that over 80% of cases have not progressed to frankly malignant disease by 10 years. In addition only about 33% at 20 years and 40% at 25 years had developed myeloma, macroglobulinaemia or lymphoma. Periodic examination of the patient and serial measurement of the concentration of the monoclonal protein are the best methods to detect the emergence of myeloma or a related disease.

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Idiopathic Bence Jones proteinuria may be a form of benign monoclonal gammopathy, but this situation is rare and we would therefore suggest that such patients should be referred. Approximately 25% of patients who continue to have the diagnosis of MGUS, which has not progressed for at least 5 years, had evidence of Bence Jones proteinuria in one series. Patients who have MGUS who do not have evidence of Bence Jones Proteinuria at presentation should have a BJP checked every couple of years. **Immunoparesis of the other immunoglobulin levels is of very real importance - if these other levels are reduced, the likelihood of this being a significant malignancy, most often myeloma is greatly increased.**

Only 4% of patients in the Mayo clinic series were under the age of 40 years.

Younger patients are a difficult group to know how to assess and manage, and we would suggest referral of patients younger than 60 irrespective of paraprotein. With advancing treatment modalities in this age group, it has become important to detect any underlying condition, such as a low-grade lymphoma or amyloidosis at the earliest possible stage.

In summary, MGUS can only be diagnosed by the exclusion of significant underlying diseases, and by demonstrating lack of progression on followup over a defined period of time. With due care and attention MGUS can be managed satisfactorily by primary care physicians. However, certain groups of patients and those in whom there is any doubt about the diagnosis should always be referred to the Haematology or Oncology department.

Reference 1: Kyle RA: Monoclonal gammopathy of undetermined significance and solitary plasmacytoma. Haematology/Oncology Clinics North America (1997) 11:71-87

Prepared by the Department of Haematology and Oncology, Christchurch Hospital, February 2000.