NATIONAL CLINICAL GUIDELINES

THE ASSESSMENT & MANAGEMENT OF COMMON ANAEMIAS IN ADULTS

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المبادئ الإرشادية السريرية لدولة قطر
NATIONAL CLINICAL GUIDELINES FOR QATAR

وزارة الصحـــــة العامـــــة
Ministry of Public Health
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2.0	Final	28th June 2020	Guidelines Team	Minor amendments to v1.0

Citation

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Abbreviations

The abbreviations used in this guideline are as follows:

AA	Aplastic anaemia
ACD	Anaemia of chronic disease
ANA	Anti-nuclear antibodies
CBC	Complete blood count
CMV	Cytomegalovirus
DAT	Direct antiglobulin test
DsDNA	Double-stranded DNA
EBV	Epstein-Barr virus
ESA	Erythropoiesis-stimulating agents
G6PD	Glucose-6-phosphate dehydrogenase
GI	Gastrointestinal
GORD	Gastro-oesophageal reflux disease
Hb	Haemoglobin
HbA	Normal adult haemoglobin
HbAS	Heterozygous combination of the normal haemoglobin gene with the sickle cell gene
HbS	Sickle haemoglobin
HbSB	Heterozygous combination of abnormal haemoglobin genes with the sickle cell gene
HbSS	Homozygous sickle cell gene
HIV	Human Immunodeficiency Virus
HRT	Hormone replacement therapy
IDA	Iron deficiency anaemia

IM	Intramuscular route
LDH	Lactate dehydrogenase
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean corpuscular volume
MDS	Myelodysplastic syndrome
MMA	Methylmalonate
NSAIDS	Non-steroidal anti-inflammatory drugs
PPI	Proton pump inhibitor
PR	Per rectum
RBC	Red blood cell
TIBC	Total iron-binding capacity

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1 Information about this Guideline

1.1 Objective and Purpose of the Guideline

The purpose of this guideline is to define the appropriate diagnosis and management of common anaemias presenting in adults. The objective is to improve the appropriateness of investigation, prescribing and referral of patients presenting to provider organisations in Qatar. It is intended that the guideline will be used primarily by physicians in primary care and outpatient settings.

1.2 Scope of the Guideline

Aspects of care covered in this guideline include the following:

- Diagnosis and management of common anaemias in adults, including:
  - Iron deficiency anaemia.
  - Thalassaemia.
  - Sickle cell haemoglobinopathies.
  - Aplastic anaemia.
  - Anaemia of chronic disease.
  - Autoimmune haemolytic anaemias.
  - Megaloblastic anaemias.

Aspects of care not covered in this guideline are:

- Anaemia in children.
- Sideroblastic anaemias.
- Non-autoimmune haemolytic anaemias.
- Detailed discussion of myelodysplastic disorders.

1.3 Editorial Approach

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this guideline, has involved the following critical steps:

- Extensive literature search for well-reputed published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising healthcare professionals, subject matter experts and patient representatives, from across Qatar.
- Independent review of the guideline by the National Clinical Guidelines & Pathways Committee, appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Whilst the MOPH has sponsored the development of the guideline, the MOPH has not influenced the specific recommendations made within it.

1.4 Sources of Evidence

The professional literature has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a member of the Editorial Team and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

1. Are designed with rigorous scientific methodology.
2. Are published in higher-quality journals.
3. Address an aspect of specific importance to the guideline in question.

Further information about the literature search and appraisal process is included in the appendix.

1.5 Evidence Grading and Recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

- **Level 1 (L1):**
  - Meta-analyses.
  - Randomised controlled trials with meta-analysis.
  - Randomised controlled trials.
  - Systematic reviews.

- **Level 2 (L2):**
  - Observational studies, examples include:
    - Cohort studies with statistical adjustment for potential confounders.
    - Cohort studies without adjustment.
    - Case series with historical or literature controls.
    - Uncontrolled case series.
  - Statements in published articles or textbooks.

- **Level 3 (L3):**
  - Expert opinion.
  - Unpublished data, examples include:
    - Large database analyses.
    - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- **Recommendation Grade A (RGA):** Evidence demonstrates at least moderate certainty of a net benefit from the recommendation.
- **Recommendation Grade B (RGB):** Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- **Recommendation Grade C (RGC):** Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- **Recommendation of the GDG (R-GDG):** Recommended best practice on the basis of the clinical experience of the Guideline Development Group members.

1.6 Guideline Development Group Members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the National Clinical Guidelines & Pathways Committee. The GDG members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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[1] Dr Ahmed Babiker attended the MOPH in his capacity as a Clinical Pharmacist and advisor on the availability of medications in Qatar.

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1.7 National Clinical Guidelines & Pathways Committee Members

The following table lists members of the National Clinical Guidelines & Pathways Committee (NCGPC), appointed by the MOPH. The NCGPC members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

National Clinical Guidelines & Pathways Committee (NCGPC) Members		
Name	**Title**	**Organisation**
Ms Huda Amer Al-Katheeri	Chair of the NCGPC, Director-Strategic Planning & Performance Department.	Ministry of Public Health
Shk Dr Mohammed Hamad J. Al Thani	Co-Chair of NCGPC, Director of Public Health	Ministry of Public Health
Prof Anthony Akobeng	Chair Clinical Practice Guidelines Committee	Sidra Medicine
Dr Alshaymaa Mohammed A. M. Al-Motawa	Consultant Family Medicine	Qatar Petroleum
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Dr Ghassan Youseph Hommos	Consultant Endocrinology	Al Emadi Hospital
Dr Egon Toft	VP and Dean of College of Medicine	College of Medicine, Qatar University

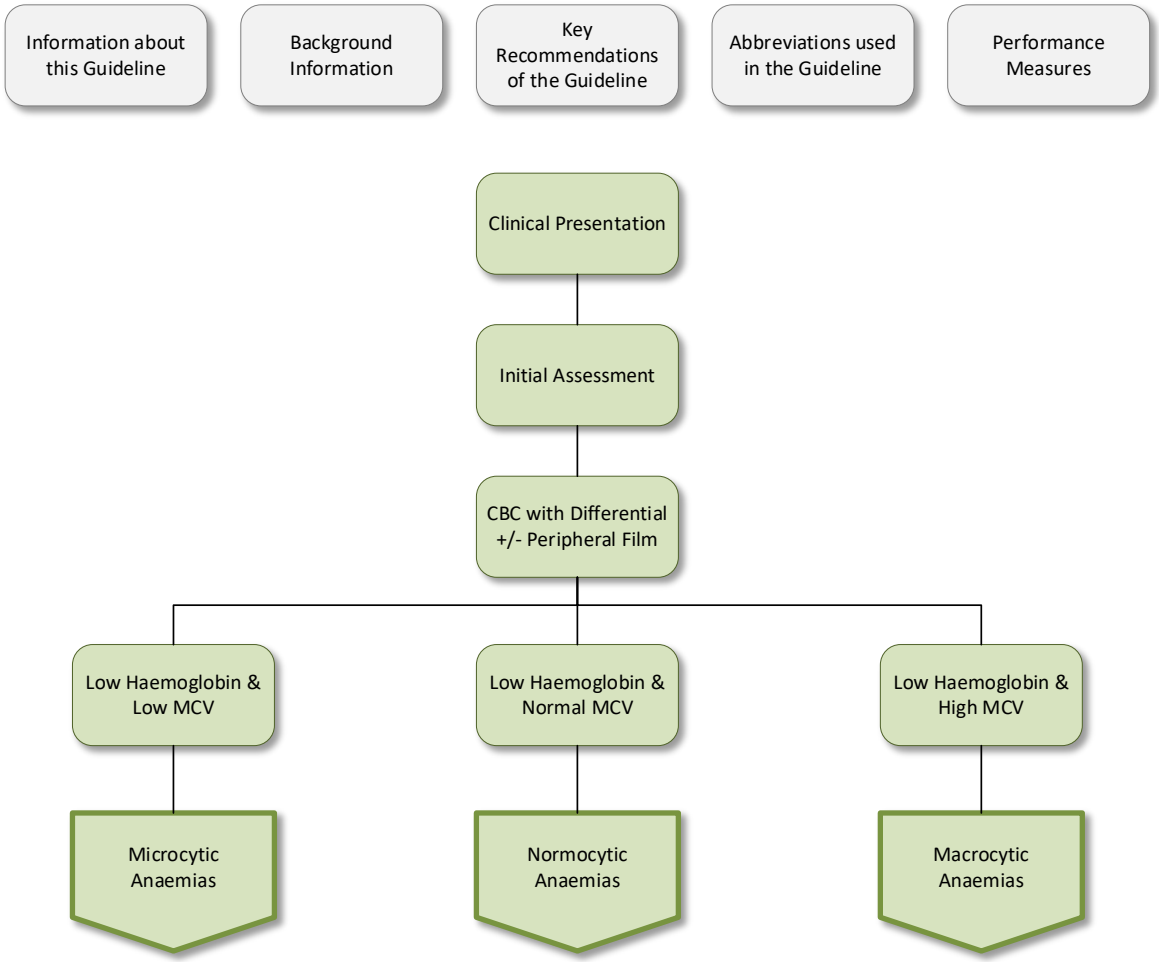
1.8 Responsibilities of Healthcare Professionals

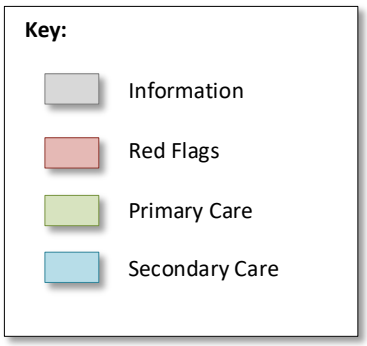
This guideline has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

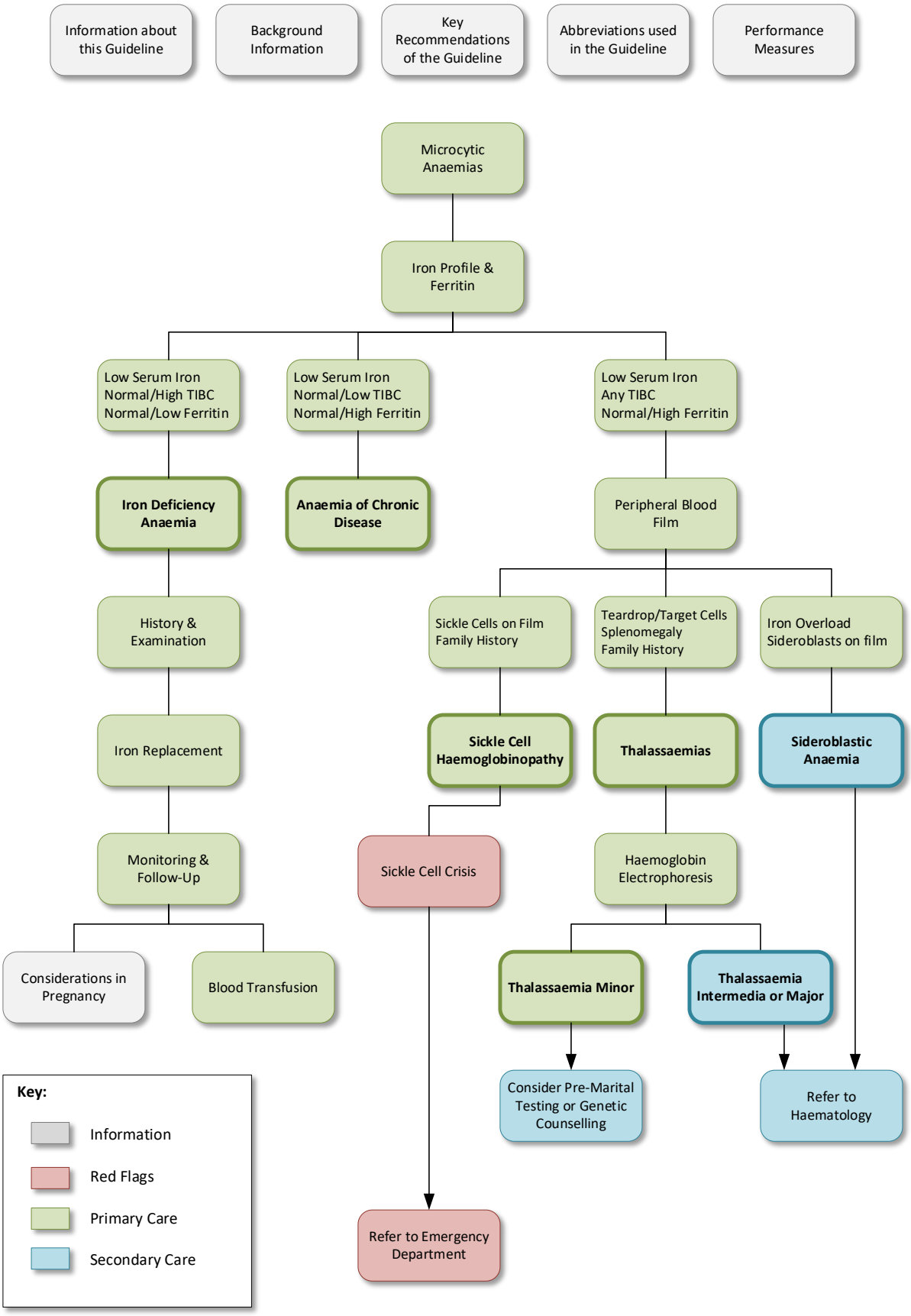
The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or caregivers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

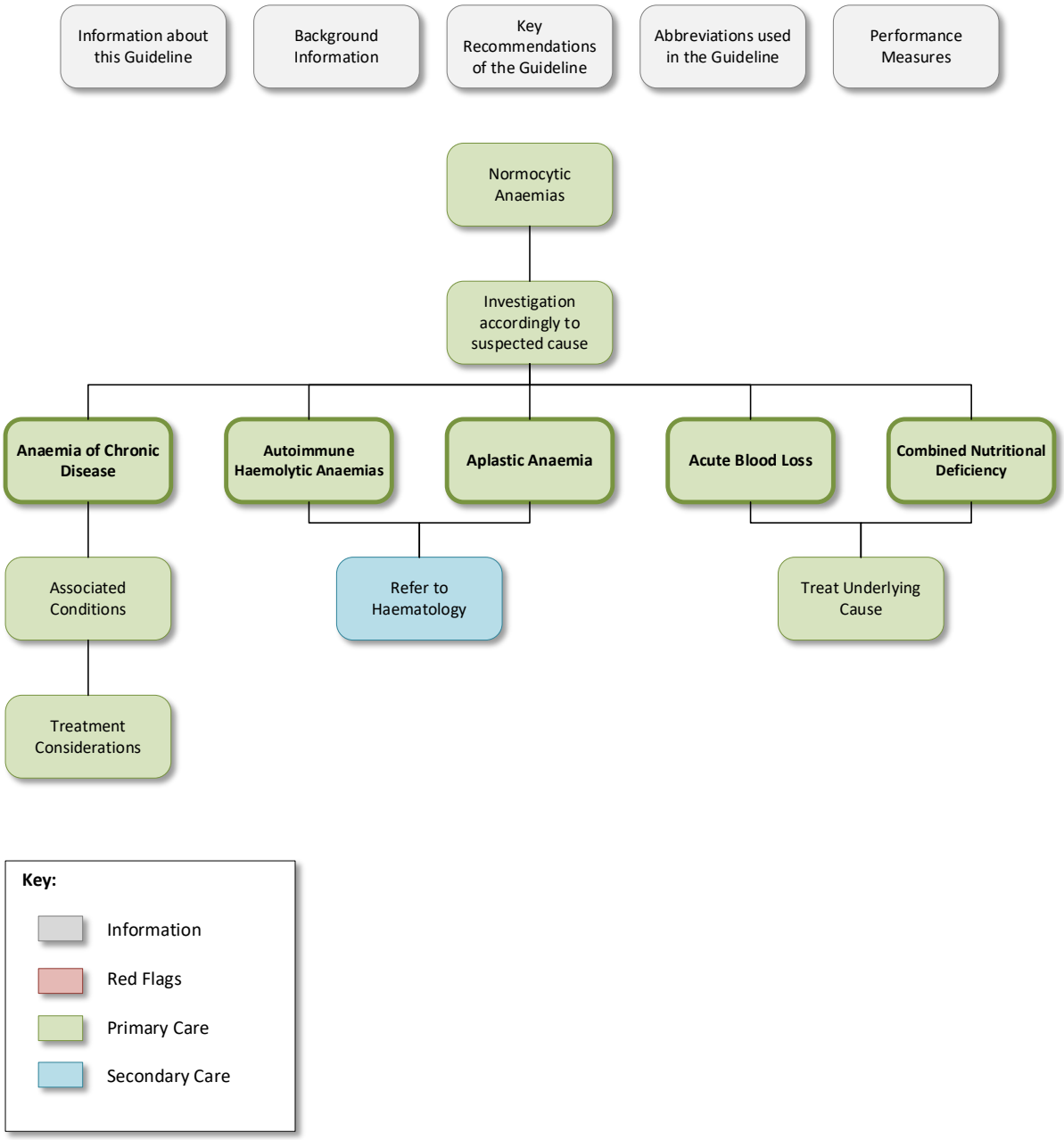
2 Common Anaemias Management Pathway

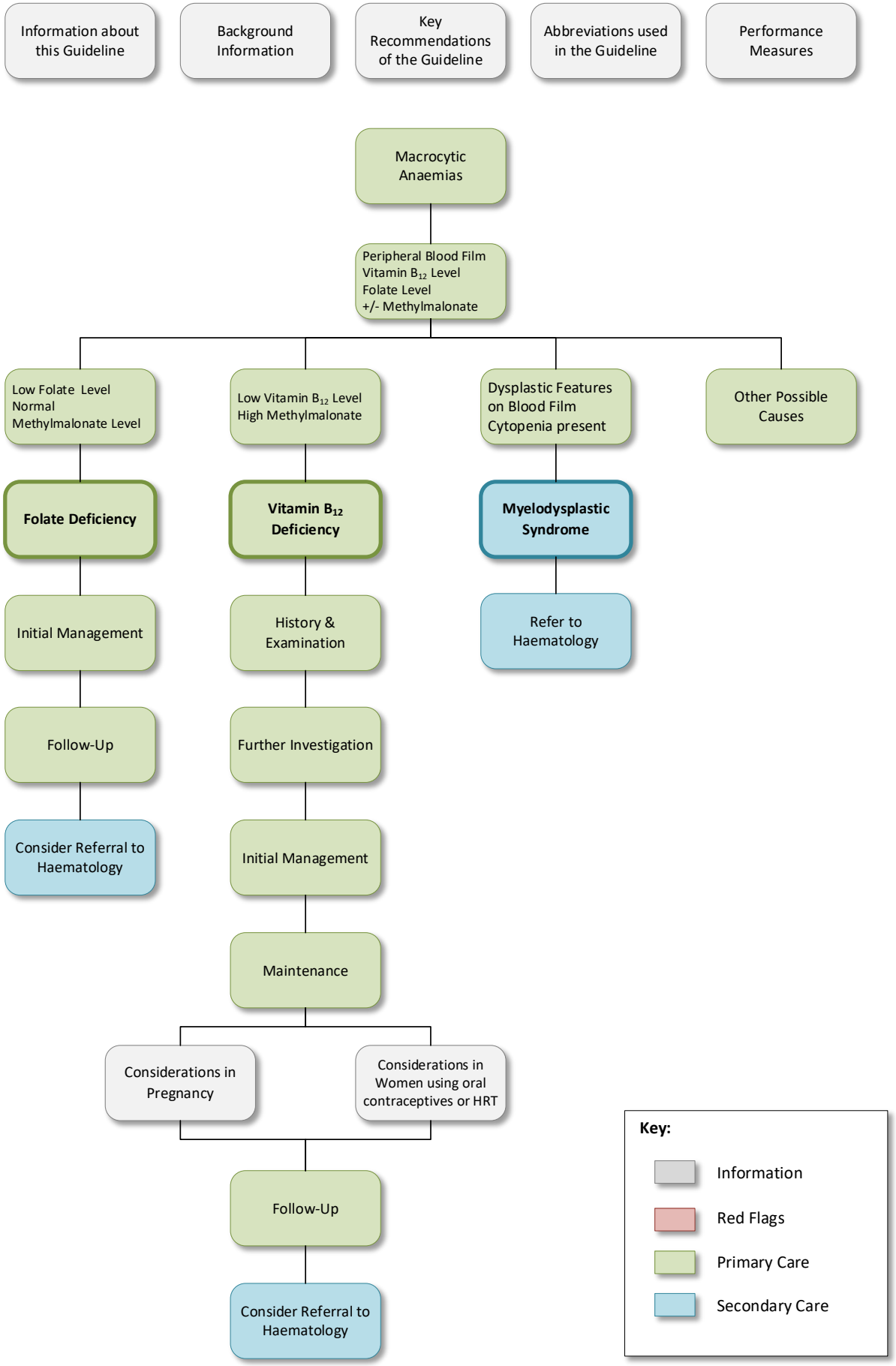
Click on a box below to see the relevant page of the Pathway.






Information about this Guideline
Background Information
Key Recommendations of the Guideline
Abbreviations used in the Guideline
Performance Measures
Microcytic Anaemias
Iron Profile & Ferritin
Low Serum Iron Normal/High TIBC Normal/Low Ferritin
Low Serum Iron Normal/Low TIBC Normal/High Ferritin
Low Serum Iron Any TIBC Normal/High Ferritin
Iron Deficiency Anaemia
Anaemia of Chronic Disease
Peripheral Blood Film
History & Examination
Sickle Cells on Film Family History
Teardrop/Target Cells Splenomegaly Family History
Iron Overload Sideroblasts on film
Iron Replacement
Sickle Cell Haemoglobinopathy
Thalassaemias
Sideroblastic Anaemia
Monitoring & Follow-Up
Sickle Cell Crisis
Haemoglobin Electrophoresis
Considerations in Pregnancy
Blood Transfusion
Thalassaemia Minor
Thalassaemia Intermedia or Major
Consider Pre-Marital Testing or Genetic Counselling
Refer to Haematology
Refer to Emergency Department
Key:
Information
Red Flags
Primary Care
Secondary Care


Information about this Guideline
Background Information
Key Recommendations of the Guideline
Abbreviations used in the Guideline
Performance Measures
Normocytic Anaemias
Investigation accordingly to suspected cause
Anaemia of Chronic Disease
Autoimmune Haemolytic Anaemias
Aplastic Anaemia
Acute Blood Loss
Combined Nutritional Deficiency
Associated Conditions
Refer to Haematology
Treat Underlying Cause
Treatment Considerations
Key:
Information
Red Flags
Primary Care
Secondary Care


Information about this Guideline
Background Information
Key Recommendations of the Guideline
Abbreviations used in the Guideline
Performance Measures
Macrocytic Anaemias
Peripheral Blood Film
Vitamin B12 Level
Folate Level
+/- Methylmalonate
Low Folate Level
Normal Methylmalonate Level
Low Vitamin B12 Level
High Methylmalonate
Dysplastic Features on Blood Film
Cytopenia present
Other Possible Causes
Folate Deficiency
Vitamin B12 Deficiency
Myelodysplastic Syndrome
Initial Management
History & Examination
Refer to Haematology
Follow-Up
Further Investigation
Consider Referral to Haematology
Initial Management
Maintenance
Considerations in Pregnancy
Considerations in Women using oral contraceptives or HRT
Follow-Up
Consider Referral to Haematology
Key:
Information
Red Flags
Primary Care
Secondary Care

3 Key Recommendations of the Guideline

The key recommendations of this guideline are:

Diagnosis:

- Anaemia is not a diagnosis and requires a full diagnostic evaluation aimed at establishing the underlying cause [1].
- Approximately 50% of anaemia in women world-wide is due to iron deficiency.
- In parts of the Eastern Mediterranean and Middle East, inherited anaemias (including sickle cell traits, G6PD deficiency and thalassaemias) are important causes of anaemia to consider [2].

Initial Investigations:

- CBC with differential [1,3,4].
- Consider performing a peripheral blood film if [1,4,5] [**R-GDG**]:
    - Anaemia is confirmed on CBC and;
    - Iron deficiency anaemia is not suspected.

Iron Deficiency Anaemia:

- Perform further investigations relevant to the underlying cause and according to the clinical scenario for confirmed Iron deficiency anaemia (IDA) (see *Section 4.2.1*).
- Unless significant overt non-GI loss is present, all postmenopausal women and male patients with confirmed IDA should be referred for an upper and lower GI investigation [5] [**L2, RGA**].
- The underlying cause of the IDA should be investigated and documented appropriately [**R-GDG**].
- In patients with a treatable underlying cause continue iron supplementation until the Hb concentration and red cell indices are normal [5,6] :
    - Continue oral iron for 3 further months until iron stores are replenished, and then stop.
    - Monitor Hb levels and red cell indices every 3 months for one year [5,6] [**L3, RGA**].
    - Recheck Hb levels once more after another year has passed and if symptoms recur.
    - If Hb or red cell indices drop below normal, give additional iron.
    - Further investigations are only indicated if Hb and red cell levels have not normalised despite treatment.

Iron Deficiency Anaemia in Pregnancy:

- Women with Hb <11g/dL (<110g/L) before 12 weeks' gestation or <10.5g/dL (<105 g/L) beyond 12 weeks' gestation, are anaemic and should be offered a trial of therapeutic iron replacement – unless they are known to have a haemoglobinopathy [7].
- Severely anaemic pregnant patients i.e. Hb levels <7g/dL (<70g/L) should be referred urgently to an obstetric specialist [7].

Thalassaemia:

- In thalassaemia minor: The Hb electrophoresis may be normal, if a coexisting iron deficiency is present. Therefore, it is important to treat any suspected iron deficiency, prior to testing for thalassaemia [**R-GDG**].
- Refer all patients to a haematologist if thalassaemia intermedia or major are suspected or confirmed [**R-GDG**].

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Sickle Cell Haemoglobinopathies:

- When sickling crises are suspected, prompt and efficient treatment remains vital and primarily consists of [8] :
    - Pain relief.
    - Oxygenation.
    - Hydration.
    - Treatment of bacterial infection or the underlying cause.
    - Transfusion may be considered after discussion with a haematologist.

Aplastic Anaemia:

- Aplastic anaemia (AA) is defined as a pancytopenia (Hb <10 g/dL, platelet count <50 x10^9/l, neutrophil count <1.5 x10^9/L), with a hypocellular bone marrow in the absence of an abnormal infiltrate or marrow fibrosis [9] .
- See *Section 11* for the initial investigations to be performed in cases of suspected AA.
- Refer all patients with suspected AA to a haematologist after exclusion of other common causes of anaemia [**R-GDG**].

Myelodysplastic Syndromes:

- Myelodysplastic syndromes (MDS) may be indicated by the following [10,11] :
    - Usually an elderly patient with macrocytic anaemia.
    - Features of dysplasia on peripheral smear.
    - Unexplained cytopenia.
- If MDS is suspected refer all cases to a haematologist for further management [**R-GDG**].

Anaemia of Chronic Disease:

- Anaemia of chronic disease (ACD) is a common cause of anaemia and is frequently associated with chronic infection or inflammatory disease states [1,12,13] .
- Patients with ACD should be referred to an appropriate specialist for management of the underlying cause [**R-GDG**].

Autoimmune Haemolytic Anaemias:

- Autoimmune haemolytic anaemias are typically indicated by [1,14] :
    - High MCV.
    - Reticulocytosis.

  NB: MCV and reticulocytes may be normal in the early stages of the disease.
    - Positive Coomb's test (direct antiglobulin test (DAT)).
- If autoimmune haemolytic anaemia is suspected on initial investigations, refer to a haematologist for further management [**R-GDG**].
- All patients with a suspected acute haemolytic crisis should however be referred to the emergency department [**R-GDG**].

Vitamin B_{12} Deficiency:

- Vitamin B_{12} deficiency is indicated by [1,15] :
    - Very high MCV.
    - Low serum vitamin B_{12} level.
    - Elevated methylmalonate level.
    - May be associated with pancytopenia.
- Investigations of vitamin B_{12} deficiency include [15,16] :

    - Testing for serum anti-intrinsic factor antibodies [15,16] [**L2**, **RGA**].
        - A positive test is associated with a high likelihood of pernicious anaemia.
- See *Section 14.1.*4 to *Section 14.1.18* for treatment and maintenance therapy in vitamin B_{12} deficiency.
- Consider seeking specialist advice from an appropriate specialist if:
    - A myelodysplastic syndrome is suspected [**R-GDG**].
    - A second opinion is required [**R-GDG**].
    - Malabsorption of vitamin B_{12}, other than pernicious anaemia, is suspected [15].
    - Patient has pernicious anaemia and gastrointestinal symptoms[15].
    - Vitamin B_{12} deficiency is thought to be due to poor diet [15].

Folate Deficiency:

- Folate deficiency is commonly seen in [6,7,15,17–19] :
    - Patients with poor dietary intake of natural sources of folate (e.g. legumes, chickpeas and brown rice).
    - Certain gastrointestinal conditions (coeliac disease, inflammatory bowel disease).
    - Blood disorders (e.g. haemolytic anaemia).
    - Pregnancy.
        - Folate requirement is increased during pregnancy.
    - Chronic alcoholism.
    - Use of anticonvulsant drugs or trimethoprim.
- See *Section 14.2.1* for the management of folate deficiency.

4 Background Information

4.1 Definitions

Anaemia is not a diagnosis and requires a full diagnostic evaluation aimed at establishing the underlying cause [1] .

Anaemia is defined as [20] :

- A condition in which the quality and/or quantity of circulating red blood cells are below normal.
- Haemoglobin (Hb) levels [3] :
    - <13g/dL (130g/L) in male patients.
    - <12g/dL (120g/L) in female patients.
    - <11g/dL (110g/L) in pregnant women.

Anaemia is typically classified on a morphological basis according to the size of erythrocytes, into the following categories [1] :

- Microcytic (MCV: <80fL).
- Normocytic (MCV: 80-100fL).
- Macrocytic (MCV: >100fL).

4.2 Aetiology

4.2.1 Microcytic Anaemia

Causes of microcytic anaemia include:

- Iron deficiency anaemia, resulting from [5–7,21,22] :
    - Chronic blood loss including:
        - Menorrhagia.
        - Epistaxis.
        - Haematuria.
        - Upper gastrointestinal (GI) bleeding.
        - Lower GI bleeding.
    - Dietary deficiency.
    - Malabsorption of iron e.g.:
        - Gastric surgery, coeliac disease, or extensive bowel resection.
    - Increased demand for iron e.g.:
        - Pregnancy.
- Anaemia of chronic disease, resulting from [1] :
    - Chronic infection e.g.:
        - Tuberculosis.
    - Chronic inflammation, including:
        - Rheumatoid arthritis
        - Systemic lupus erythematosus.
        - Polymyalgia rheumatica.
        - Malignancy.
- Sideroblastic anaemia, resulting from [1] :
    - Inherited disease:
        - X-linked inheritance.
    - Acquired disease:

        - Myelodysplasia.
        - Myeloproliferative disorders.
        - Myeloid leukaemia.
        - Rheumatoid arthritis.
        - Malignancy.
        - Drugs e.g. isoniazid.
        - Alcohol misuse.
        - Lead toxicity.
- Thalassaemias [1] .

4.2.2 Normocytic Anaemia

Normocytic anaemia may result from [12] :

- Increased red blood cell loss or destruction.
- Decreased red cell production.

Causes of normocytic anaemia due to **increased red blood cell loss or destruction** include [1,12,14,17,23,24] :

- Acute blood loss.
- Hypersplenism.
- Haemolytic disorders:
    - Congenital conditions:
        - Haemoglobinopathies e.g., homozygous sickle cell disease (haemoglobin SS disease); heterozygous sickle haemoglobin C disease (haemoglobin SC disease).
        - Disorders of red cell membranes e.g., hereditary spherocytosis, hereditary elliptocytosis.
        - Red blood cell enzyme deficiencies e.g., Glucose-6-phosphate dehydrogenase deficiency, pyruvate kinase deficiency.
    - Mechanical haemolysis:
        - Macrovascular disorders e.g., history of heart valve replacement or valvular disorder.
        - Microangiopathic disorders e.g., disseminated intravascular coagulopathy, haemolytic-uraemic syndrome, thrombotic thrombocytopenic purpura.
    - Autoimmune haemolytic anaemias:
        - Warm-reactive anaemias.
        - Cold-reactive anaemias.
        - Drug-induced anaemias.
    - Paroxysmal nocturnal haemoglobinuria.
- Drugs that can cause haemolysis, e.g.:
    - Penicillin.
    - Methyldopa.
    - Cephalosporins.
    - Erythromycin.
    - Procainamide.
    - Paracetamol.
- Infections.
- Blood transfusion reactions.

Causes of normocytic anaemia due to **decreased red cell production** may include [1,3,12,17,20,25] :

- Primary causes:
    - Marrow aplasia or hypoplasia.
    - Pure red blood cell aplasia.
    - Myelophthisis.
    - Myeloproliferative disorders.
- Secondary causes:
    - Chronic renal failure.
    - Liver disease.
    - Endocrine deficiencies.
    - Inflammatory disorders.
    - Infections.
    - Cancer.
    - HIV.
- Drugs:
    - Antiepileptic medications.
    - Azathioprine.
    - Sulphonamides.
    - Isoniazid.
    - Procainamide.
    - Penicillamine.
    - Chloramphenicol.
- Expansion of plasma volume:
    - Pregnancy.
    - Over-hydration.

4.2.3 Macrocytic Anaemia

Common causes of macrocytic anaemia include [1,12,25,26] :

- Vitamin B_{12} or folate deficiency.
- Excess alcohol intake - may cause macrocytosis more commonly due to toxic effect of alcohol than folate deficiency secondary to alcoholism.
- Pregnancy and the neonatal period.
- Drugs, e.g.:
    - Azathioprine.
    - Hydroxycarbamide.
    - Methotrexate.
    - Anticonvulsants (phenytoin, valproic acid).
    - Trimethoprim/sulfamethoxazole.
    - Metformin.
    - Cholestyramine.
    - Zidovudine.
    - Stavudine.
    - Lamivudine.
- Hypothyroidism – modest increase in mean cell volume may be seen.
- Liver disease (non-alcoholic).
- Haemolysis.

Rarer causes include [1,3,24,26] :

- Myeloma.
- Myelofibrosis.
- Myelodysplastic syndrome.

- Bone marrow failure syndromes, e.g. aplastic anaemia, red cell aplasia.
- Primary bone marrow dysplasias including myelodysplasia and myeloproliferative disorders.

4.3 Epidemiology

Definitive data on the incidence and prevalence of anaemia in Qatar is not presently available. However, the 2011 WHO-estimated percentages of women with anaemia were as follows [2] :

- Non-pregnant women aged 15-49 years:
  - Hb <12g/dL (<120g/L): 28%.
  - Hb <8g/dL (<80g/L): 0.7%.
- Pregnant women aged 15-49 years:
  - Hb <11g/dL (<110g/L): 28%.
  - HB <7g/dL (<70g/L): 0.2%.

Approximately 50% of anaemia in women world-wide is due to iron deficiency. In parts of the Eastern Mediterranean and Middle East, inherited anaemias (including sickle cell traits, G6PD deficiency and thalassaemias) are important causes of anaemia to consider [2] .

5 Clinical Presentation

Presenting features are common to most anaemias [7,20,23,24,27,28] :

- Common symptoms:
  - Fatigue, lethargy, weakness.
  - Shortness of breath.
  - Palpitations.
  - Headache.
  - Lightheadedness or dizziness.
- Less common symptoms:
  - Tinnitus.
  - Taste disturbance.
  - Pruritus.
  - Pica: Abnormal cravings for non-food items, e.g. ice, sand, paint or starch.
  - Sore tongue.
  - Brittle nails.
  - Hair loss.
  - Restless legs syndrome.

6 Initial Assessment

Consider asking about the following:

- Dietary history [5,6,29,30] [**L1**]:
  - Vegans and vegetarians or patients on other restricted diets.
  - Alcohol intake.
- GI ulceration/bleeding [1,5,6,29,31] [**L1**]:
  - NSAIDs, aspirin, corticosteroid or anticoagulant use.
  - Dyspepsia, GORD, history of peptic ulcer.

    - Haemorrhoids.
    - Passing blood per rectum (PR).
    - Passing black motions, confirm they are not taking iron tablets.
    - Personal or family history of:
        - Telangiectasia or angiodysplasia.
        - Coagulopathies.
        - Inflammatory bowel disease.
- Malabsorption [5,22] [**L2**]:
    - History of GI diseases, gastrectomy or bariatric surgery.
    - Symptoms including: indigestion, diarrhoea, steatorrhoea, abdominal distention.
- Menstrual history [1,24] :
    - Frequency, duration, estimated blood loss.
    - Obstetric history.
    - Post-menopausal bleeding.
- Haematuria [6,21] **.**
- Epistaxis [5,7] .
- Parasitic infestations [32] .

Consider performing a general physical examination, as directed by the clinical presentation. Features to examine for include [1,4–6,28,33,34] :

- Assess pallor of conjunctivae, mucus membranes and palms.
- Assess for:
    - Stomatitis and cheilitis.
    - Atrophic glossitis.
    - Nail changes - brittle, ridged koilonychia.
- Look for cutaneous signs such as jaundice, petechiae, bruising, telangiectasia, or rare causes of GI blood loss, e.g. Peutz-Jeghers syndrome and hereditary haemorrhagic telangiectasia [1,5,23,35] .
- Cardiovascular examination:
    - Signs of heart failure, infective endocarditis, prosthetic heart valves, tachycardia, postural hypotension.
- Neurological examination:
    - Signs of peripheral neuropathy or cognitive impairment.
- Rectal examination:
    - PR bleeding, melaena, rectal masses, haemorrhoids.

7 Initial Investigation of Anaemia

7.1 Initial Investigation

Initial investigations for anaemia [1,3,4] :

- CBC with differential.

Consider performing a peripheral blood film if [1,4,5] [**R-GDG**]:

- Anaemia is confirmed on CBC and;
- Iron deficiency anaemia is not suspected.

View Pathway

7.2 Further Investigation and Diagnosis

Use the algorithm in *Figure 7.2* to guide further investigation and diagnosis of the anaemia [**R-GDG**].
Each of the common diagnoses is discussed in further detail in the subsequent sections.

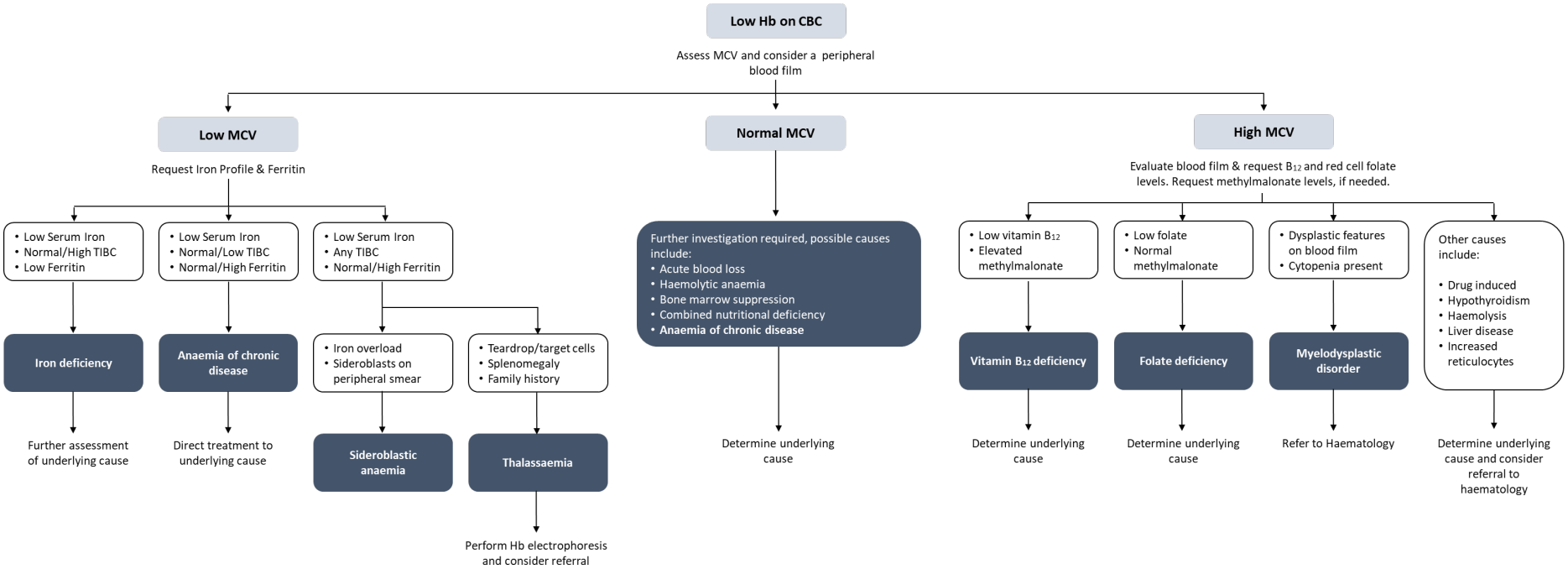

Figure 7.2: Algorithm for the Investigation of Anaemia [1,4,5] .

View Pathway

8 Iron Deficiency Anaemia

Iron deficiency anaemia is indicated by [1,4–6,24] :

- Low MCV (<80fL).
- Low MCH and low MCHC.
- Microcytic hypochromic red cells on peripheral blood film.
- Low serum iron.
- High TIBC.
- Low ferritin.

8.1 History and Examination

Determine whether the following supporting features in the history are present:

- Review of general presenting symptoms, ask about [7,20,20,24,30] :
    - Shortness of breath.
    - Fatigue or lethargy.
        - Energy level and response to exertion.
    - Palpitations.
    - Headache.
    - Hair loss.
- Family history of iron deficiency anaemia (IDA), haematological disorder, telangiectasia, and bleeding disorders [5] .
- Menstrual history [1,24,36] :
    - Frequency, duration, estimated blood loss.
    - Obstetric history.
- Post-menopausal bleeding [21] .
- Malabsorption [5,22] :
    - History of gastrectomy or other bariatric procedures.
    - Symptoms of coeliac disease e.g., indigestion, diarrhoea, abdominal distention.
- GI ulceration/bleeding [4–6,19,24,31,37] :
    - NSAIDs or aspirin use.
    - Dyspepsia, indigestion, history of peptic ulcer.
    - Haemorrhoids.
    - Passing blood PR.
    - Passing melaena.
- Dietary history [5,6,30] :
    - Vegans and vegetarians have an increased risk of IDA.
    - Persons eating a normal, well balanced diet including meat, green vegetables, and iron fortified meals are unlikely to have dietary IDA.
- Possible malignancy [21,38,39] :
    - Unintentional weight loss.
    - Dysphagia.
    - Change of bowel habit.
    - Abdominal pain.
    - Abdominal mass.
    - Passing mucus PR.
    - Tenesmus.
    - Family history of bowel cancer.
- History of blood donation or any other blood loss [5] .
- Haemodialysis [30] .
- Haematuria [6,21] .
- Epistaxis [5,6] .

- Heavy hookworm infestation (travel to tropical countries) [37] .
- Medication history e.g. use of PPI or H_2 receptor antagonists [38] .

Assess for signs, causes and complications of iron deficiency, including [4,6,28,33,34,37] :

- Angular stomatitis.
- Angular cheilitis.
- Atrophic glossitis.
- Brittle, ridged nails or koilonychia.
- Telangiectasia, or rare causes of GI blood loss, e.g. Peutz-Jeghers syndrome and hereditary haemorrhagic telangiectasia.
- Cardiovascular examination:
    - Signs of heart failure, infective endocarditis, prosthetic heart valves, tachycardia, postural hypotension.
- Rectal examination:
    - PR bleeding, melaena, rectal masses, haemorrhoids.

8.3 Further Investigation

Perform further investigations relevant to the underlying cause and according to the clinical scenario for confirmed IDA (see *Section 4.2.1*).

Unless significant overt non-GI loss is present, all postmenopausal women and male patients with confirmed IDA should be referred for an upper and lower GI investigation [5] [**L2, RGA**].

8.4 Management

8.4.1 Iron Replacement

The underlying cause of the IDA should be investigated and documented appropriately [**R-GDG**]. Once a cause has been identified, first-line treatment with iron replacement restores iron and normalises Hb and red blood cells. Also provide advice about diet [5,7,36] [**L1**].

Iron supplementation [5–7,36,38] :

- Oral supplements to replace iron.
    - Ascorbic acid may enhance iron absorption.
- Take 1 hour before meals on an empty stomach.
- Assess compliance and response to oral iron after 2-4 weeks with CBC; and serum ferritin after 4 weeks:
    - If well tolerated, continue iron for a minimum of 3 months.
    - Patients should undergo specialist assessment if there is a lack of response (i.e. Hb increase of <2g/dL (<20g/L)) after 2-4 weeks of adherence to treatment.

If poorly tolerated (e.g. symptoms of epigastric discomfort, nausea, diarrhoea or constipation), consider the following actions [6,6,7,36] :

- Offer advice that adverse effects should settle down with time, stressing the importance of compliance.
- Offer a laxative to patients with constipation.
- Offer reassurance to patients with black stools as a consequence of iron use.

- Reduce the frequency of dosing to once per day, if necessary.
- Prescribe alternative iron compounds (e.g. ferrous fumarate, ferrous gluconate, ferrous glycinate) or formulations (iron suspensions), which may be tolerated better than ferrous sulphate.

If the person is still unable to tolerate oral iron supplements, consider parenteral iron [5] :

- Parenteral iron may be used when:
    - There is intolerance or non-compliance with oral preparations.
    - Patients have had gastric surgery or procedures resulting in malabsorption of iron.

NB: Be aware that oral iron may adversely reduce absorption of other medications [1] .

8.4.2 Follow-Up

In patients with a treatable underlying cause continue iron supplementation until the Hb concentration and red cell indices are normal [5,6] :

- Continue oral iron for 3 further months until iron stores are replenished, and then stop.
- Monitor Hb levels and red cell indices every 3 months for one year [5,6] [**L3, RGA**].
- Recheck Hb levels once more after another year has passed and if symptoms recur.
- If Hb or red cell indices drop below normal, give additional iron.
- Further investigations are only indicated if Hb and red cell levels have not normalised despite treatment.

Ongoing iron supplementation may be beneficial in some patients who [36] :

- Have recurring anaemia and in whom further investigations are not indicated or appropriate.
- Those who habitually eat an iron-poor diet and are unlikely to change.
- Have malabsorption.
- Have menorrhagia.
- Are pregnant.
- Have had a gastrectomy.
- Are undergoing haemodialysis.

8.4.3 Blood Transfusions

Reserve blood transfusions for patients who have not responded to iron therapy and are at risk of cardiovascular instability [5] [**L3, RGA**]. This includes patients who are due to have endoscopic investigations before response to iron therapy is expected.

8.4.4 Considerations in Pregnant Patients with IDA

Women with Hb <11g/dL (<110g/L) before 12 weeks' gestation or <10.5g/dL (<105 g/L) beyond 12 weeks gestation, are anaemic and should be offered a trial of therapeutic iron replacement – unless they are known to have a haemoglobinopathy and have no evidence of concomitant iron deficient state[7].

Severely anaemic patients i.e. Hb levels <7g/dL (<70g/L) patients should be referred urgently to an obstetric specialist [7] .

View Pathway

9 Thalassaemias

Thalassaemias are indicated by [1,4–6] :

- Low MCV (<80fL).
- Teardrop red cells on peripheral blood film.
- Target cells.
- Splenomegaly may be present.
- Positive family history may be present.

NB: If thalassaemia is suspected a haemoglobin electrophoresis should be performed [5] .

9.1 Classification and Management

Thalassaemias are inherited disorders of globin chain synthesis that result in ineffective erythropoiesis and may result in haemolysis. The thalassaemias are common amongst people of Mediterranean, Middle Eastern and South Asian ethnicity [1,5] .

Thalassaemias may be classified according to the affected globin chain [35] :

- Beta-thalassaemia.
- Alpha- thalassaemia.

Thalassaemias may be classified into the following clinical syndromes [1] :

- Thalassaemia minor.
- Thalassaemia intermedia.
- Thalassaemia major.

Thalassaemia Minor [1] :

- Heterozygous alpha or beta-thalassaemia.
- Patients are symptomless.
- Anaemia is mild or absent on CBC.
- No treatment is necessary unless the patients have coincidental haematological pathology.
- If a coexisting iron deficiency anaemia is present, the Hb electrophoresis may be normal. Therefore, it is important to treat any suspected IDA, prior to testing for thalassaemia [**R-GDG**].
- Pre-marital testing and genetic counselling may be indicated [**R-GDG**].

Thalassaemia Intermedia [1] :

- May be due to a range of causes of impaired globin chain synthesis.
- Patients may be symptomatic with moderate anaemia (Hb: 7-10g/dL (70-100g/L)).
- Splenomegaly and bone deformities may be present.
- Recurrent leg ulcers, gallstones and infections are also seen.
- Refer all patients to a haematologist for specialist review and management [**R-GDG**].

Thalassaemia Major [1] :

- Patients are usually identified at neonatal screening or when they present with failure to thrive in their first year of life.
- Severe anaemia is present on CBC.
- Radiographic findings include: ‘hair on end’ appearance of bone.
- Refer all suspected cases to a haematologist for specialist review and management [**R-GDG**].

View Pathway

10 Sickle Cell Haemoglobinopathies

Sickle cell haemoglobinopathies are indicated by the following [8,40] :

- Analysis of haemoglobin using Hb electrophoresis.
- Deformation or sickling of red cells under conditions of hypoxia, acidity and cellular dehydration.
- Microvascular occlusion, sepsis, haemolysis and ischaemia of tissues (sickling crisis).

10.1 Classification and Management

Sickle haemoglobin (HbS) is a structural variant of normal adult haemoglobin (HbA) characterised by an abnormal beta-globulin chain. This abnormality causes red blood cells to distort into a sickle shape when deoxygenated [38] .

Sickle cell haemoglobinopathy can be classified according to the inherited gene into[8,40]:

- **Sickle Cell Anaemia:**
  - Homozygous for sickle cell gene (HbSS).
- **Sickle Cell Disease:**
  - Heterozygous combination of abnormal haemoglobin genes with the sickle cell gene (HbSB).
- **Sickle Cell Trait:**
  - Heterozygous combination of the normal haemoglobin gene with the sickle cell gene (HbAS).

Sickle Cell Anaemia or Disease [8,40] :

- Suspect this in high-risk ethnic groups who present with:
  - Acute painful crises.
  - Infection (bacterial sepsis).
  - Anaemia (pallor).
  - Stroke.
  - Priapism.
  - Chest pain, cough and fever (acute chest syndrome).

Sickle Cell Trait[8,40] :

- Rarely have symptoms.
  - Symptoms are possible under acute stress, including:
    - Severe dehydration.
    - Severe hypoxia.
    - Severe infections.
    - General anaesthesia.

When sickling crises are suspected, prompt and efficient treatment remains vital and primarily consists of[8]:

- Pain relief.
- Oxygenation.
- Hydration.
- Treatment of bacterial infection or the underlying cause.
- Transfusion may be considered after discussion with a haematologist.

View Pathway

11 Aplastic Anaemia

Aplastic anaemia (AA) is defined as a pancytopenia (Hb <10 g/dL, platelet count <50 $x10^9$/l, neutrophil count <1.5 $x10^9$/L), with a hypocellular bone marrow in the absence of an abnormal infiltrate or marrow fibrosis [9] .

Depending on blood count and findings from bone marrow aspiration, AA can be classified according to the *Camitta criteria* into the following categories [9] [**L1, RGA**]:

- Non-severe.
- Severe.
- Very severe.

AA can be inherited or acquired and in the majority of cases a definitive cause remains unknown (idiopathic). When AA is suspected, assess for [9,41] :

- Drug history.
- Occupational history.
- Family history.
- History of viral infection e.g. hepatitis, HIV.

Initial investigation of suspected AA, should include [9] :

- Peripheral smear.
- Reticulocyte count.
- Vitamin B_{12} and folate levels.
- Liver function tests.
- Viral serology (Hepatitis A, B and C, EBV, CMV, HIV and parvovirus B19).
- Anti-nuclear antibodies (ANA) and anti-dsDNA.
- Chest radiograph.
- Abdominal ultrasound scan.
- Echocardiogram.

NB: Refer all patients with suspected AA to a haematologist after exclusion of other common causes of anaemia [**R-GDG**].

View Pathway

12 Anaemia of Chronic Disease

Anaemia of chronic disease is indicated by [1,12,13] :

- Low or normal MCV.
- Low serum iron.
- Normal or low TIBC
- Normal or elevated serum ferritin.

12.1 Associated Chronic Diseases

Anaemia of chronic disease (ACD) is a common cause of anaemia and is frequently associated with chronic infection or inflammatory disease states, including [1,12,13] :

- Chronic kidney disease.
- Chronic heart disease.
- Tuberculosis.
- Rheumatoid arthritis.
- Systemic lupus erythematosus.
- Crohn's disease.
- Polymyalgia rheumatica.
- Malignancy.

12.2 Treatment Considerations

Treatment considerations [1,13,17] :

- Patients do not respond to iron therapy and treatment should be directed at the underlying cause.
- The level of anaemia correlates with the activity of the underlying disease and treatment of the underlying disease can improve the anaemia.

Consider RBC transfusion [13,20] :

- For treatment of severe or life-threatening anaemia.
- Where the patient has symptomatic anaemia; or
- A co-morbid disorder for which a moderately low Hb level imposes additional risk.

Erythropoiesis-stimulating agents (ESAs) [13,19,20] :

- May be appropriate in a subset of patients with ACD.
- Rule out iron deficiency prior to initiating therapy.
- Consider iron therapy to patients receiving ESA maintenance therapy.
- Before a decision on whether or not to continue with ESA treatment is made, review patients after agreed intervals.

NB: Patients with ACD should be referred to an appropriate specialist for management of the underlying cause [**R-GDG**].

View Pathway

13 Autoimmune Haemolytic Anaemias

Autoimmune haemolytic anaemias are typically indicated by [1,14] :

- High MCV.
- Reticulocytosis.
- NB: MCV and reticulocytes may be normal in the early stages of the disease.
- Positive Coomb's test (direct antiglobulin test (DAT)).

Other findings that may be present include [1,14] :

- Splenomegaly.
- Abnormal red cells on peripheral smear.
    - Spherocytosis.
    - Polychromasia.
    - Anisopoikilocytosis.
- Raised lactate dehydrogenase (LDH).
- Raised indirect bilirubin with normal alanine transaminase (ALT).
- Low haptoglobin.

13.1 Aetiology

Causes include [1,14] :

- Cold antibody:
    - Idiopathic causes.
    - Secondary causes.
- Warm antibody:
    - Idiopathic causes.
    - Secondary causes.

13.2 Clinical Presentation

In addition to the symptoms and signs of anaemia described in *Section 5*, patients may also present with[1]:

- Splenomegaly.
- Jaundice.
- Haemoglobinuria.
- Acute haemolytic crisis:
    - Fever.
    - Rigors.
    - Back pain.
    - Abdominal pain.
    - Shock.

13.3 Further Investigation

Further investigation may include [14] :

- Viral serology.
- Autoimmune screen.
- Cold agglutinin titres.
- Abdominal ultrasound.
- Chest radiograph, if indicated.

If autoimmune haemolytic anaemia is suspected on initial investigations, refer to a haematologist for further management [**R-GDG**]. All patients with a suspected acute haemolytic crisis should however be referred to the emergency department [**R-GDG**].

14 Macrocytic Anaemias

If suspected, the following investigations should be performed in addition to a CBC and a peripheral smear[26] :

- Reticulocyte count.
- LDH.
- Methylmalonate level (MMA).
- Homocysteine.
- Vitamin B_{12}.
- Red cell folate level.

Further investigations which may be indicated by the clinical presentation [15] :

- Intrinsic factor antibodies.
- Anti-transglutaminase antibodies.
- Anti-endomysial antibodies.
- Anti-parietal cell antibodies.

14.1 Vitamin B_{12} deficiency

Vitamin B_{12} deficiency is indicated by [1,15,19]:

- Very high MCV.
- Low serum vitamin B_{12} level.
- Elevated MMA level.
- May be associated with pancytopenia.

14.1.1 History and Examination

If a vitamin B_{12} deficiency is suspected, ask about the following [6,12,15,18,19,26] :

- Neurological symptoms, e.g.:
    - Numbness.
    - Poor motor coordination.
    - Memory lapses.
    - Dorsal cord syndromes:
        - Bilaterally symmetrical ataxia.
        - Paraesthesia.
        - Age-related cognitive impairment.
- Psychological symptoms, particularly depression.
- Drug history.
- Dietary history: prolonged vegan diet.
- Alcohol intake.

Examine for the following [15,16,19,26,42] :

- Signs of vitamin B_{12} deficiency:
  - Glossitis.
  - Oropharyngeal ulceration.
  - Neuropsychiatric signs:
    - Irritability.
    - Depression.
    - Psychosis.
    - Cognitive impairment.
  - Poor responses to:
    - Vibration.
    - Touch.
    - Pain.
    - Position.
  - Visual disturbance – optic atrophy.
  - Abnormal gait.
  - Subacute combined degeneration of the spinal cord:
    - Joint position and vibration sense are usually first to be affected, with lower limb weakness and ataxia occurring if the person is not treated.
    - Classic triad of signs – extensor plantar reflexes, brisk knee reflexes, absent ankle reflexes.

14.1.2 Aetiology

Underlying causes of vitamin B_{12} deficiency include [15,18,19] :

- Pernicious anaemia:
  - Malabsorption of vitamin B_{12} due to lack of intrinsic factor.
  - Often familial (30% of cases have a positive family history).
- Other causes include:
  - Gastrectomy.
  - Gastric bypass surgery.
  - Bariatric surgery.
  - Ileal resection.
  - Autoimmune disorders, e.g. Crohn's disease.
  - HIV.
  - Inadequate dietary intake, e.g. due to veganism.
- The following drugs are associated with, or can cause, vitamin B_{12} deficiency [25] :
  - Metformin.
  - Proton pump inhibitors (PPIs).
  - H_2 receptor antagonists.
  - Trimethoprim-sulfamethoxazole.
  - Phenytoin.
  - Neomycin.
  - Colchicine.
  - Combined oral contraceptive pill.

14.1.3 Investigations

Investigations of vitamin B_{12} deficiency include [15,16] :

- Testing for serum anti-intrinsic factor antibodies [15] [**L2**, **RGA**].
    - A positive test is associated with a high likelihood of pernicious anaemia.

When measuring serum vitamin B_{12} note the following:

- Interpreting results should not be done in isolation and must include clinical features and other laboratory values [15,16] [**L2**, **RGB**]:
    - Normal levels do not rule out clinically significant vitamin B_{12} deficiency (especially in elderly patients).
    - Pregnant women may have low levels due to increased plasma volume.

14.1.4 Initial Management

If neurological symptoms are present, initial treatment will comprise of [19,25] :

- Intramuscular (IM) injections of hydroxocobalamin every second day, until improvement is no longer the case.
- NB: After 3 weeks of treatment, review the need for continuation of alternate day therapy.

If neurological symptoms are not present, initial treatment will comprise of [19,25] :

- IM hydroxocobalamin every other day for 2 weeks.
- Oral hydroxocobalamin [19,25] :
    - May be considered in cases where malabsorption is not a cause.
    - May be considered to correct or maintain suboptimal levels in asymptomatic patients [19] [**L3, RGA**].
    - May be given to patients with vitamin B_{12} levels of subclinical deficiency on two occasions for 4 weeks [19] [**L1, RGA**].
    - In the event of neuropathy symptoms, patients should be advised to seek medical attention [19] [**L2, RGA**].
    - Recheck levels after 3 months and consider second-line tests if there is no improvement [19] [**L2, RGA**].

14.1.5 Maintenance Treatment

When the underlying cause is not dietary, maintenance treatment includes [15,19,25] :

- Lifelong IM injections of hydroxocobalamin at intervals of 2-3 months.
- In patients with neurological symptoms, it is currently not recommended to give oral cobalamin.

When the underlying cause is dietary, maintenance treatment includes [15,19,43] :

- Daily oral hydroxocobalamin tablets taken between meals; or
- Hydroxocobalamin injection given twice a year − may be preferable in those who are more likely to have malabsorption such as the elderly.
- In vegans, this treatment may need to be life-long.
- In non-vegan patients, once vitamin B_{12} levels have been corrected and diet has improved, treatment can be terminated.
- Advise consumption of foods rich in vitamin B_{12}, e.g.:
    - Meat, eggs, and dairy products.

- Foods fortified with vitamin B_{12} – for example soy products, most breakfast cereals and breads.

- Patients with a history of bariatric surgery [19] :
  - Are likely to need some replacement therapy [19] [**L1, RGA**].
  - Low dose oral replacement therapy may be beneficial to patients with food-bound cobalamin malabsorption [19] [**L2, RGA**].

14.1.6 Considerations in Pregnant Patients

Considerations in pregnant patients [15,19] :

- Vitamin B_{12} levels fall during pregnancy due to increased plasma volume. Measurements are therefore less reliable in determining deficiency [19] [**L1**].
- There is no gold standard to test for vitamin B_{12} deficiency in pregnancy; however, MMA and homocysteine tests are sensitive and specific indicators of functional vitamin B_{12} deficiency [29] .
- A short course of empirical hydroxocobalamin should be given in the event of strong clinical features of deficiency [15] [**L2, RGA**]:
  - Further investigations should be conducted post-partum.

14.1.7 Considerations in Women on Oral Contraception or HRT

Asymptomatic women taking oral contraception or hormone replacement therapy (HRT) with mildly reduced serum vitamin B_{12} (110-148pmol/L), should be advised [19] [**L2, RGA**]:

- To review their dietary intake of cobalamin-rich foods.
- Cobalamin supplements may be considered.

14.1.8 Follow-Up

Follow-up will comprise of [15,19] :

- CBC and reticulocyte count after two weeks:
  - There should be a rise in the Hb level and an increase in the reticulocyte count.
  - If there is no improvement:
    - Check serum folate level (if this has not already been done).
    - Review the initial diagnosis.
- Confirm a normal CBC after 2-3 months of treatment.
- Monitoring.
  - Patients treated with a 4-week trial of oral hydroxocobalamin should have their vitamin B_{12} level rechecked after 3-4 months [19] [**L2**]:
  - If there is no improvement, consider referral for further evaluation.
  - Continued monitoring, beyond this period, is generally considered to be unnecessary, although there are a few exceptions such as [15] :
    - Suspected lack of compliance with treatment.
    - Recurrence of anaemia.

14.1.9 Consider Referral

Consider seeking specialist advice from an appropriate specialist if:

- A myelodysplastic syndrome is suspected [**R-GDG**].
- A second opinion is required [**R-GDG**].

- Malabsorption of vitamin B_{12}, other than pernicious anaemia, is suspected [15] .
- Patient has pernicious anaemia and gastrointestinal symptoms [15] .
- Vitamin B_{12} deficiency is thought to be due to poor diet [15] .

14.2 Folate Deficiency

Folate deficiency is indicated by [1,15,19] :

- Very high MCV.
- Low folate levels.
- Normal methylmalonate levels.

Folate deficiency is commonly seen in [7,15,17–19,22] :

- Patients with poor dietary intake of natural sources of folate (e.g. legumes, chickpeas and brown rice).
- Certain gastrointestinal conditions (coeliac disease, inflammatory bowel disease).
- Blood disorders (e.g. haemolytic anaemia).
- Pregnancy.
    - Folate requirement is increased during pregnancy.
- Chronic alcoholism.
- Use of anticonvulsant drugs or trimethoprim.

14.2.1 Management of Folate Deficiency

Management of folate deficiency [15,19,25,43] :

- Oral folic acid is used to treat folate deficiency in order to replenish body stores if inadequate dietary intake is the cause.
- A treatment course for 4 months is usually sufficient however longer treatment is recommended if the underlying cause of folate deficiency persists.
- If treated concurrently for vitamin B_{12} deficiency, treatment should be initiated with cobalamin therapy before adding in folate therapy.
- Prophylactic folate therapy is indicated in:
    - Chronic haemolytic states.
    - Malabsorption conditions.
    - Patients on renal dialysis.
    - Pregnancy to prevent neural tube defects.
        - Oral folic acid is offered to pregnant women with a known folate deficiency, in the preconception period and until term, to avoid risk of neural tube defects in the child.
    - Patients who experience side effects secondary to methotrexate use.

14.2.2 Follow-Up

Follow up of patients prescribed folic acid treatment [15] :

- Perform CBC and reticulocyte count checks at:
    - 10 days after treatment to determine a response.
    - 8 weeks to confirm normalization of CBC.

View Pathway

14.2.3 Consider Referral

Consider seeking specialist advice from an appropriate specialist if [15] :

- The patient has neurological symptoms.
- The patient is pregnant.
- The patient has another underlying haematological disorder [**R-GDG**].
- Malabsorption of folate is suspected.
- Antibody testing suggests coeliac disease.
- If folate deficiency is considered to be due to poor diet.

14.3 Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) may be indicated by the following [10,11] :

- Usually an elderly patient with macrocytic anaemia.
- Features of dysplasia on peripheral smear.
- Unexplained cytopenia.

NB: If MDS is suspected refer all cases to a haematologist for further management [**R-GDG**].

15 Key Considerations for Patient Preferences

Patient preferences refer to patient perspectives, beliefs, expectations, and goals for health and life, and to the steps employed by individuals in assessing the potential benefits, harms, costs, and limitations of the management options in relation to one another. Patients may have preferences when it comes to defining their problems, identifying the range of management options and selecting or ranking the outcomes used to compare these options.

It is important for healthcare professionals to develop an understanding of the patient as an individual and the unique way in which each person experiences a condition and its impact on their life.

The following recommendations are therefore made for physicians and other healthcare professionals regarding general principles of patient care in Qatar. All clinicians and health care practitioners involved in patients' care in the State of Qatar should:

- **Respect Patients:** Treat patients with respect, kindness, dignity, courtesy and honesty. Ensure that the environment is conducive to discussion and that the patient's privacy is respected, particularly when discussing sensitive, personal issues. Ask the patient how they wish to be addressed and ensure that their choice is respected and used.

- **Maintain Confidentiality:** Respect the patient's right to confidentiality and avoid disclosing or sharing patients' information without their informed consent. In this context, students and anyone not directly involved in the delivery of care should first be introduced to the patient before starting consultations or meetings, and let the patient decide if they want them to stay.

- **Clarify Third-Party Involvement:** Clarify with the patient at the first point of contact whether and how they like their partner, family members or carers to be involved in key decisions about their care or management and review this regularly. If the patient agrees, share information with their partner, family members or carers.

- **Obtain Informed Consent:** Obtain and document informed consent from patients, in accordance with MOPH policy and guidance.

- **Encourage Shared Decision Making:** Ensure that patients are involved in decision making about their own care, or their dependent's care, and that factors that could impact the patient's participation in their own consultation and care including physical or learning disabilities, sight, speech or hearing impairments and problems with understanding, reading or speaking English are addressed.

- **Disclose Medical Errors:** Disclose errors when they occur and show empathy to patients.

- **Ensure Effective Communication:** Explore ways to improve communication including using pictures, symbols or involving an interpreter or family members. Avoid using medical jargon. Use words the patient will understand and confirm understanding by asking questions.

Ensure Continuity of Care: Provide clear and timely sharing of patient information between healthcare professionals especially at the point of any transitions in care.

16 Performance Measures

A performance measure is given in the table below. Healthcare organisations are encouraged to monitor service performance using the indicator definitions below [44].

Number	Numerator	Denominator
CA01	Number in the denominator who are referred to gastroenterology for investigation of an underlying cause.	Total number of male patients ≥18 years and female postmenopausal patients, with iron deficiency anaemia but without overt non-gastrointestinal bleeding.

Table 16.1: Performance measure [44].

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Appendix A: Detailed Description of the Literature Search

A systematic search for existing literature on common anaemias was performed in the period April 3rd – April 9th, 2020.

All existing references were evaluated and where necessary and applicable, the latest version of the specific manuscript was used to update the guideline and replace the older reference. The search for clinical practice guidelines on common anaemias assessment and/or management was performed in the *PubMed* database and websites of relevant organizations and societies including the *British Society of Haematology*, the *World Health Organization* the *Royal College of Surgeons* and the *American Society of Haematology*. The present guideline is primarily based on *UK NICE*, the *European Society for Medical Oncology* and the *American Academy for Family Physicians* guidelines and is supplemented with other relevant studies.

Peer-reviewed scientific publications were found in PubMed and via *Google Scholar* Internet search engine. Non-peer reviewed studies were identified in *bioRxiv*. Books were checked on *Amazon* and via *Google* and *Google Scholar* search engines.

The included publications were identified using the terms "Anaemia" and specified with the following terms in combinations:

Guideline, epidemiology, adult, aetiology, definition, prevalence, assessment, investigation, diagnosis, microcytic, normocytic, macrocytic, iron deficiency, vitamin B12, folate, magaloblastic, haemolytic, autoimmune, aplastic, sickle cell, chronic, pregnancy, examination, diagnosis, differential diagnosis, symptoms, classification, management, prevention, treatment, transfusion, referral, specialist, follow-up.

Figure A.1 below demonstrates graphically the results of the search and application of exclusion criteria.

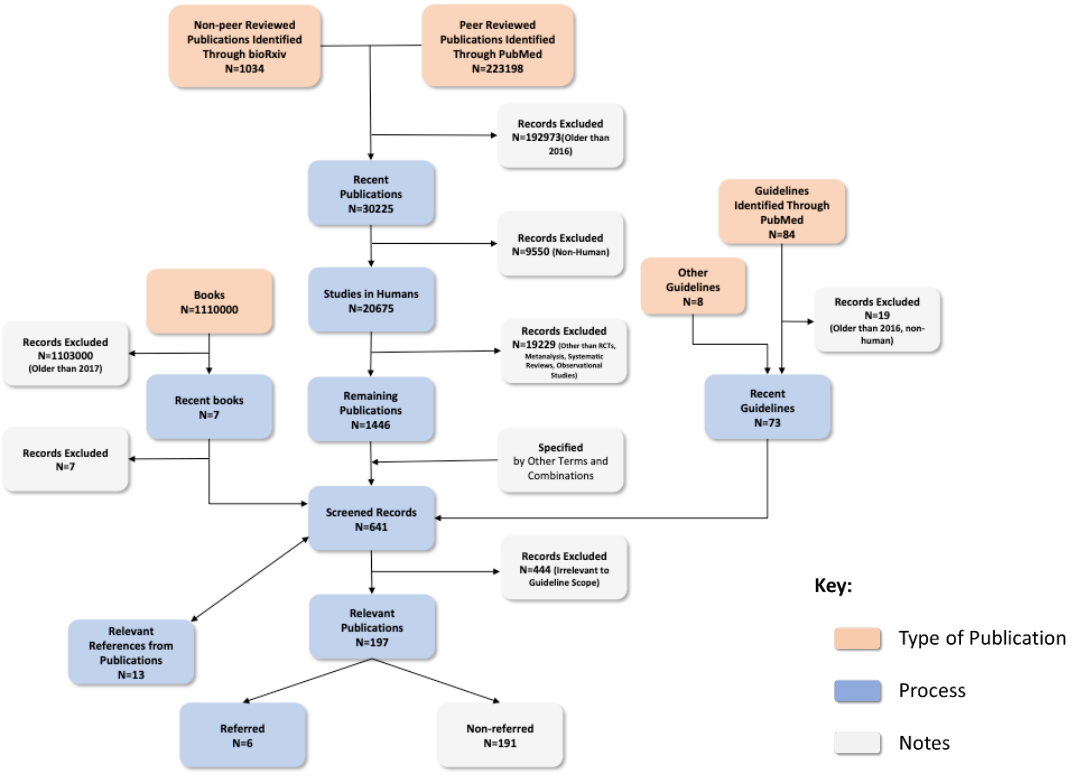

Fig A.1: Literature search results and application of exclusion criteria.

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