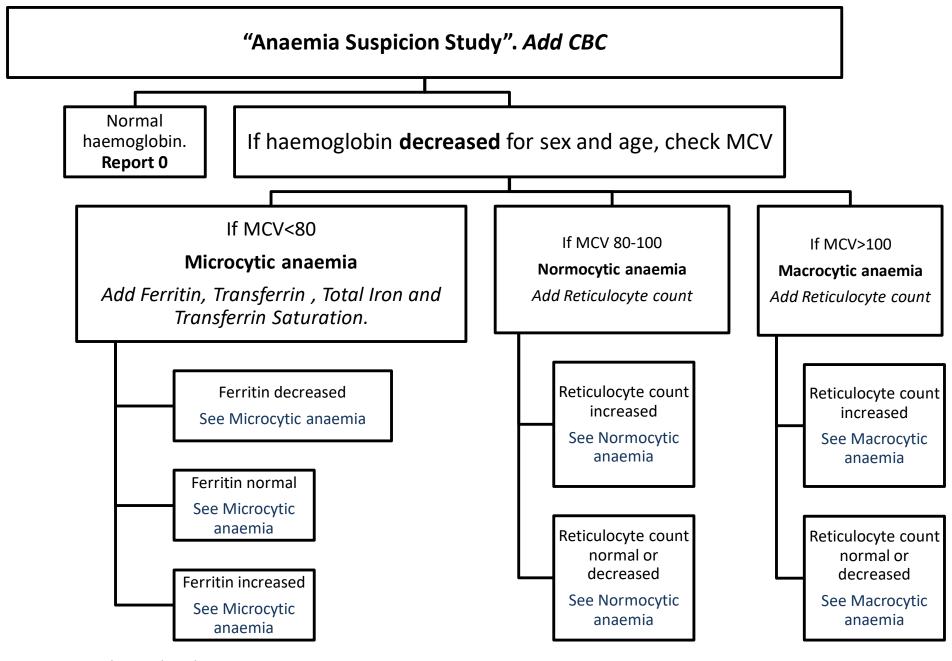
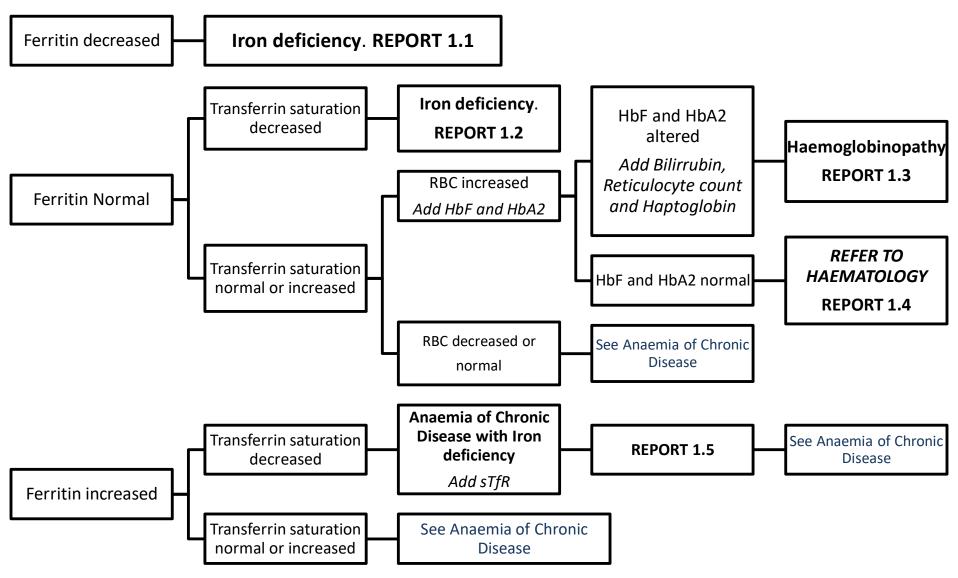
Supplementary data

Primary Care Anaemia Algorithm Strategy



CBC: Complete Blood Count; MCV: Mean corpuscular volume

Microcytic anaemia algorithm



HbF: Fetal haemoglobin; HbA2: A2

haemoglobin; RBC: Red Blood Cell count; sTfR:

Serum Transferrin Receptor

Microcytic Anaemia Reports

Report 1.1: Iron deficiency anaemia

"Due to the low result of haemoglobin and the presence of microcytosis we have studied the iron profile in the patient. Low ferritin suggests iron deficiency. We recommend initiating treatment and monitor in one month".

Report 1.2: Iron deficiency anaemia

"Due to the low result of haemoglobin and the presence of microcytosis we have studied the iron profile in the patient. Low transferrin saturation (even with normal ferrtin) suggests iron deficiency. We recommend initiating treatment and monitor in one month".

Report 1.3: Haemoglobinopathy

"Due to the low result of haemoglobin, the presence of microcytosis, normal results for iron profile and increased RBC count, we have studied haemoglobin fractions with the following results suggestive of an haemoglobinopathy. *Description of the results*.

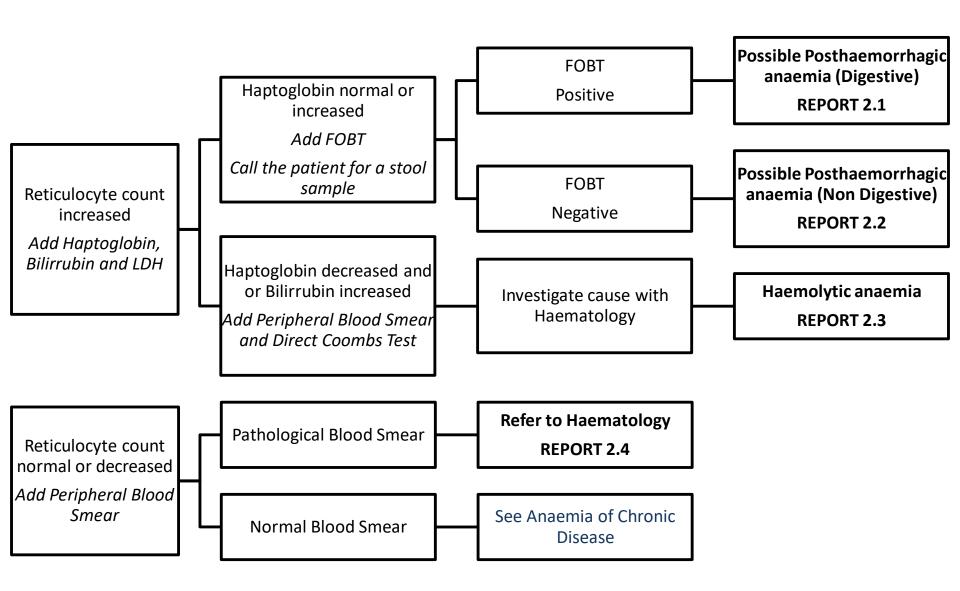
Report 1.4: Refer to Haematologist

"Due to the low result of haemoglobin, the presence of microcytosis, normal results for iron profile and increased RBC count, we have studied haemoglobin fractions. The results are not suggestive of an haemoglobinopathy so we recommend referring the patient to Haematology Department for consultation".

Report 1.5: Anaemia of Chronic Disease with Iron deficiency anaemia

"Due to the low result of haemoglobin and the presence of microcytosis we have studied the iron profile in the patient. Results suggest the presence of a mixed anaemia (chronic disease and iron deficiency). Ferritin is an acute phase reactant and its concentrations are increased in states of inflammation. We have also studied sTfr. Because sTfR is insensitive to inflammation, it can detect anaemia in patients with preexisting inflammatory states, and is particularly useful in distinguishing between the anaemia of chronic disease and anaemias caused by lack of iron intake where its concentrations are increased. ".

Normocytic Anaemia algorithm



FOBT: Faecal Occult Blood Test

Normocytic Anaemia Reports

Report 2.1: Possible Posthaemorrhagic anaemia (Digestive)

"Due to the low result of haemoglobin, normocytosis, an increased reticulocyte count and high levels of Haptoglobin we could rule out the presence of an haemolytic anaemia. In order to know if there is an underlying haemorrhagic process we have studied FOCBT obtaining a positive result. We recommend referring the patient to Digestive Tract Department for consultation and blood transfusión if the blood loss is acute and/or haemoglobin very low (<7 g/dL)".

Report 2.2. Possible Posthaemorrhagic anaemia (Non Digestive)

"Due to the low result of haemoglobin, normocytosis, an increased reticulocyte count and high levels of Haptoglobin we could rule out the presence of an haemolytic anaemia. In order to know if there is an underlying haemorrhagic process we have studied FOCBT obtaining a negative result. We recommend studying the origin of blood loss (being recent surgery, trauma, renal or gynecologic origin, the main causes) and blood transfusión if the blood loss is acute and/or haemoglobin very low (<7 g/dL)".

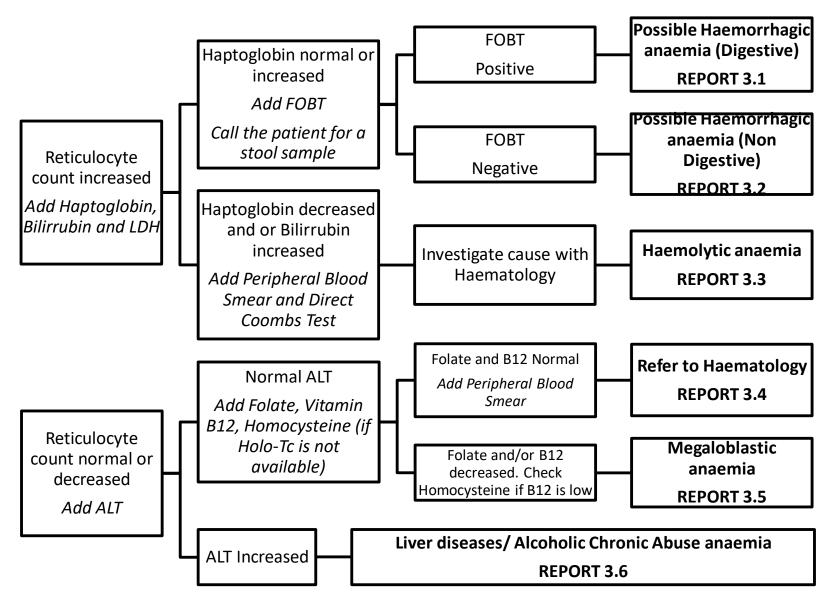
• Report 2.3. Haemolytic anaemia

"A low result of haemoglobin, normocytosis, an increased reticulocyte count and low levels of Haptoglobin are highly suggestive of the presence of an haemolytic anaemia. We have performed a Peripheral Blood Smear and Direct Coombs Test for confirmation. Results from Haematology Department are attached."

Report 2.4. Refer to Haematologist

"Due to the low result of haemoglobin, normocytosis, an normal/decreased reticulocyte count we have performed a Peripheral Blood Smear. Our findings are compatible with an haematologic disease. Results from Haematology Department are attached. We recommend referring the patient to Hematology Department for further studies."

Macrocytic Anaemia algorithm



ALT: alanine transaminase; Holo-Tc: Holo Transcobalamin

Macrocytic Anaemia Reports

Report 3.1: Possible Posthaemorrhagic anaemia (Digestive)

"Due to the low result of haemoglobin, macrocytosis, an increased reticulocyte count and high levels of Haptoglobin we could rule out the presence of an haemolytic anaemia. In order to know if there is an underlying haemorrhagic process we have studied FOCBT obtaining a positive result. We recommend referring the patient to Digestive Tract Department for consultation and blood transfusión if the blood loss is acute and/or haemoglobin very low (<7 g/dL)".

Report 3.2. Possible Posthaemorrhagic anaemia (Non Digestive)

"Due to the low result of haemoglobin, macrocytosis, an increased reticulocyte count and high levels of Haptoglobin we could rule out the presence of an haemolytic anaemia. In order to know if there is an underlying haemorrhagic process we have studied FOCBT obtaining a negative result. We recommend studying the origin of blood loss (being recent surgery, trauma, renal or gynecologic origin, the main causes) and blood transfusion if the blood loss is acute and/or haemoglobin very low (<7 g/dL)".

• Report 3.3. Haemolytic anaemia

"A low result of haemoglobin, macrocytosis, an increased reticulocyte count and low levels of Haptoglobin are highly suggestive of the presence of an haemolytic anaemia. We have performed a Peripheral Blood Smear and Direct Coombs Test for confirmation. Results from Haematology Department are attached."

Report 3.4. Refer to Haematologist

"Due to the low result of haemoglobin, macrocytosis, and normal values of ALT, Folate and Vitamin B12, we have performed a Peripheral Blood Smear. Results from Haematology Department are attached. We recommend referring the patient to Haematology Department for further studies."

Macrocytic Anaemia Reports

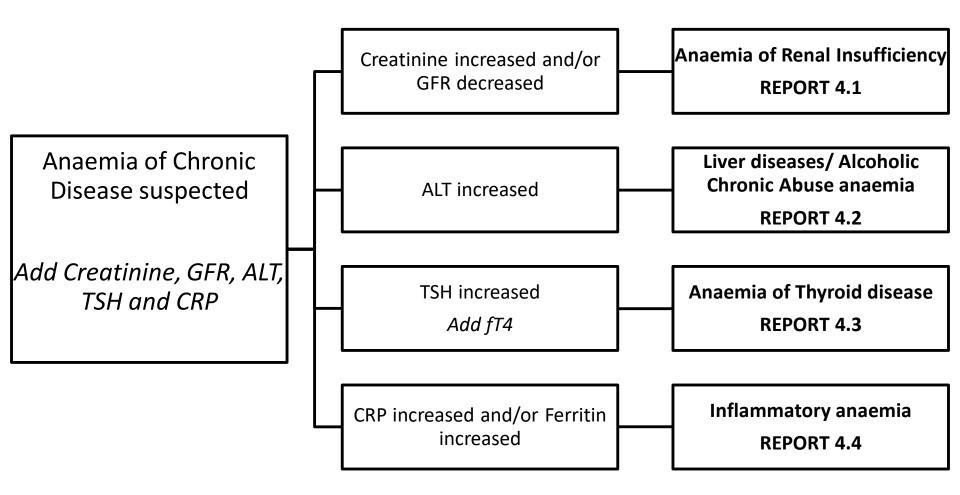
Report 3.5. Megaloblastic anaemia

"A low result of haemoglobin, macrocytosis, normal values of ALT, and decreased levels of Folate and/or Vitamin B12 are highly suggestive of megaloblastic anaemia. We recommend initiating treatment and monitor in one month".

Report 3.6. Liver diseases/ Alcoholic Chronic Abuse anaemia

"A low result of haemoglobin, macrocytosis, normal values of Folate and/or Vitamin B12 and increased results of ALT are highly suggestive of anaemia due to chronic liver diseases. We recommend searching for the cause of this hepatopathy in order to treat it properly. Alcohol abuse could be a potential cause of anaemia in these patients. Don't forget that alcohol produces macrocytosis through a direct toxicity mechanism on blood cell precursors. Alcohol's indirect effects include nutritional deficiencies that impair the production and function of various blood cells."

Anaemia of Chronic Disease algorithm



ALT: alanine transaminase; fT4: free thyroxine;

GFR: Glomerular Filtration Rate, CRP: C – Reactive Protein; TSH: Thyroid-stimulating

hormone

Anaemia of Chronic Disease Reports

Report 4.1: Anaemia of Renal Insufficiency

"The results suggest the presence of anaemia related to an underlying chronic disease with renal insufficiency being the most plausible explanation due to the increased creatinine levels and/or low GFR rate. The anaemia associated with anaemia of chronic disease is usually mild. Treating the underlying disease that is causing the anaemia is the first step to treating most forms of anaemia of chronic disease. In many cases, treating these diseases will resolve the anaemia and its symptoms."

Report 4.2. Liver diseases/ Alcoholic Chronic Abuse anaemia

"The results suggest the presence of anaemia related to an underlying chronic disease with liver disorder being the most plausible explanation due to the increased ALT levels. We recommend searching for the cause of this hepatopathy in order to treat it properly. Alcohol abuse could be a potential cause of anaemia in these patients. Don't forget that alcohol produces macrocytosis through a direct toxicity mechanism on blood cell precursors. Alcohol's indirect effects include nutritional deficiencies that impair the production and function of various blood cells."

Report 4.3. Anaemia of Thyroid disease

"The results suggest the presence of anaemia related to an underlying chronic disease with thyroid disease being the most plausible explanation due to the increased TSH levels and/or low fT4. The anaemia associated with anaemia of chronic disease is usually mild. Treating the underlying disease that is causing the anaemia is the first step to treating most forms of anaemia of chronic disease. In many cases, treating these diseases will resolve the anaemia and its symptoms."

Report 4.4. Inflammatory anaemia

"The results suggest the presence of anaemia related to an underlying chronic disease with an inflammatory state being the most plausible explanation due to the increased CRP and/or ferritine levels. The anaemia associated with anaemia of chronic disease is usually mild. Treating the underlying disease that is causing the anaemia is the first step to treating most forms of anaemia of chronic disease. In many cases, treating these diseases will resolve the anaemia and its symptoms."

Threshold values used

- haemoglobin:
 - Female: 11.5 15.5 g/dL
 - Male: 12.0 16.0 g/dL
- Ferritin:
 - Female: 10 120 ng/mL
 - Male: 20 300 ng/mL
- Folate: > 2.8 ng/mL
- Total iron: $50 150 \mu g/dL$
- Transferrin: 200 360 mg/dL
- Transferrin saturation: 20 50 %
- Vitamin B12: 197 866 pg/mL