Factsheet
Anaemia

CPPE
CENTRE FOR PHARMACY POSTGRADUATE EDUCATION

Contents

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Definition

The World Health Organization (WHO) defines anaemia as *'a condition in which the number of red blood cells or the haemoglobin concentration within them is lower than normal.'1 This reduces their oxygen carrying capacity which may be insufficient to meet physiological needs. 'The optimal haemoglobin concentration needed to meet physiologic needs varies by age, sex, elevation of residence, smoking habits and pregnancy status.'[1] Anaemia can be caused by nutritional deficiencies (mainly iron, vitamin B12 or folate), or other causes.*

WHO has produced ***Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity***. This outlines haemoglobin levels that can be used to aid a diagnosis of anaemia. In this summary anaemia is defined as:

Men (15 years of age and above)	less than 130 g/litre
Non-pregnant women (15 years of age and above)	less than 120 g/litre
Pregnant women[2]	less than 110 g/litre

(Table taken from WHO, *Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity[2])*

Access the WHO document for haemoglobin levels in children.

Anaemia may be classified based on the red blood cell (RBC) size and haemoglobin content

The following video, and the pictorial illustration in the table below, explain the different classifications of anaemia (please note that the reference range for haemoglobin levels in men is slightly different to the WHO guidance,[1] but the main principles are the same).

Armando Hasudungan – Anaemia, classification (microcytic, normocytic and macrocytic) and pathophysiology

RBC size		
Microcytic	Normocytic	Macrocytic
		
Low mean cell volume (MCV)	Normal MCV	High MCV

Haemoglobin content		
Hypochromic	Normochromic	Hyperchromic
		
Low haemoglobin	Normal haemoglobin	High haemoglobin

Anaemia may be classified based on the cause

Iron deficiency is the most common cause of anaemia. It leads to diminished RBC production due to low body iron stores. This is the most common cause of microcytic and hypochromic anaemia.[3,4]

Vitamin B12 and folate deficiency leads to the abnormal development and production of RBCs. This is the most common cause of megaloblastic (large faulty RBCs) anaemia.[5] The most common cause of this is pernicious anaemia, an autoimmune condition resulting in an inability to absorb vitamin B12.[6]

Aplastic anaemia is a result of decrease in all blood cell production by the bone marrow. RBCs are one of the types of blood cells affected.[4]

Haemolytic anaemia is a result of RBCs surviving for less than the normal 120 days in circulation.[4]

Anaemia of chronic disease occurs in long-term conditions, such as such as ***chronic kidney disease***, inflammatory diseases and chronic infection, and leads to reduced blood cell production.[7]

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Prevalence and incidence

Iron deficiency

Iron deficiency anaemia is thought to affect around 500 million people worldwide, and is more prevalent in less economically developed countries. Incidence is highest in women during childbearing years due to menstruation and pregnancy. In the UK, prevalence is estimated to be 23 percent in pregnant women and 14 percent in non-pregnant women.[8]

Vitamin B12 and folate deficiency

In the UK the prevalence of vitamin B12 deficiency is around 6 percent in people aged less than 60 years; this rises to around 20 percent in those over 60 years. Pernicious anaemia has a mean age of onset of 60

years among white people. In black people this average age of onset is lower at 50 years, but this is skewed due to an increased occurrence in young black women.[9]

Aplastic anaemia
The incidence of aplastic anaemia is around two per million people per year in North America and Europe. There are two peaks in incidence at 10 to 25 years then again at over 60 years.[10]

Haemolytic anaemia and anaemia of chronic diseases
The prevalence and incidence of haemolytic anaemia and anaemia of chronic diseases is variable due to variability in underlying cause.[11,12]

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Signs and symptoms

Anaemia symptoms generally develop over time and may go unnoticed. General symptoms of anaemia include:

- fatigue
- lethargy
- breathlessness
- feeling faint
- headaches
- pale skin
- palpitations
- tinnitus
- loss of appetite and weight loss.[13]

There are then symptoms specific to the following three types of anaemia (iron deficiency, vitamin B12 and folate deficiency and aplastic anaemia) shown in the table on the next page.
(Patients who present with these symptoms require referral to their GP)

Those with haemolytic anaemia tend to present with features of the underlying cause[14], and those with anaemia of chronic diseases tend to present with features of the underlying disorder.[15]

Visit CPPE's ***Biochemistry*** gateway page and access the *Iron deficiency anaemia case study* short e-learning programme. The case study follows someone who presents with symptoms of iron deficiency anaemia.

Iron deficiency: • tiredness and lack of energy • shortness of breath • noticeable heartbeats (heart palpitations) • pallor (pale skin) and less commonly: • pica (abnormal food cravings, eg, dirt/ice) • food tasting strange • pruritus (feeling itchy) • a sore tongue • hair loss • ***dysphagia*** • angular cheilosis (ulcers in the corners of mouth) • koilonychia (spoon-shaped nails) • restless legs syndrome.[16,17]	**Vitamin B12 and folate deficiency:** Symptoms of vitamin B12 deficiency: • mild jaundice • glossitis (smooth and sore tongue) • mouth ulcers • changes in gait • irritability • ***depression*** • numbness and tingling in the feet and hands *Neurological complications*: • loss of sensation • loss of mental and physical drive • muscle weakness • optic neuropathy • psychiatric disturbances ranging from mild neurosis to severe dementia • neuropathy • urinary or faecal incontinence. Symptoms of folate deficiency: • reduced sense of taste • diarrhoea • numbness and tingling in the feet and hands • muscle weakness • depression.[13,19]	**Aplastic anaemia:** In this case symptoms will reflect cytopenia (low number of mature blood cells): • infection from leukopenia (low white blood cells) • fatigue, pallor, exertional dyspnoea • tachycardia from anaemia • bleeding or easy bruising from thrombocytopenia (low platelets).[18]

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Causes/risk factors

Iron deficiency

Iron deficiency anaemia is usually due to multiple factors. Dietary deficiency can contribute, however this is rarely the only cause (iron is mainly found in meat, seafood and vegetables).[20] Other factors include:

- malabsorption
- increased blood loss – in men and post-menopausal women blood loss is likely to be due to a gastrointestinal bleed (which would require an urgent referral for investigation and could be drug induced eg, by NSAIDs). In pre-menopausal women this is mostly caused by menstrual blood loss
- increased requirements - for example, growth in children, adolescence and pregnancy.[20,21]

For more information access the National Institute of Health and Care Excellence (NICE) clinical knowledge summary (CKS) ***Anaemia - iron deficiency, Causes***.

Vitamin B12 and folate deficiency

Vitamin B12 is absorbed through the stomach lining after binding with a glycoprotein called intrinsic factor (IF). IF is produced by parietal cells which are found in the lining of the stomach.

Pernicious anaemia, an autoimmune disease, is the most common cause of vitamin B12 deficiency. In pernicious anaemia, parietal cell antibodies are produced which attack the parietal cells. Parietal cell antibodies can be detected via a blood test.[22]

Other causes of deficiency include:

- medicines such as methotrexate, colchicine, metformin, nitrous oxide, proton pump inhibitors and H2-receptor antagonists
- gastric abnormalities, eg, total or partial gastrectomy
- genetic factors
- issues that affect intestinal absorption, eg, Crohn's Disease
- malnutrition and vegan diets – vitamin B12 is found mainly in food that comes from animals such as milk, cheese, eggs, fish, shellfish and meat (note that it becomes more difficult to absorb vitamin B12 as you get older).[21,22,23]

Aplastic anaemia

Aplastic anaemia often develops spontaneously or in associate with another condition, although occasionally it may be caused by a toxin such as exposure to benzene, dipyrone, non-steroidal anti-inflammatory drugs (NSAIDs), chloramphenicol (oral), penicillamine, and gold.[24]

Haemolytic anaemia

Haemolytic anaemia may be genetic or acquired. The website ***Patient*** offers information on haemolytic anaemia aimed at medical professionals.

Anaemia of chronic diseases

It is thought that the inflammation that is usually present in chronic disease leads to decreased RBC production due to a fall in serum iron, and often shortened RBC life spans.[25,26]

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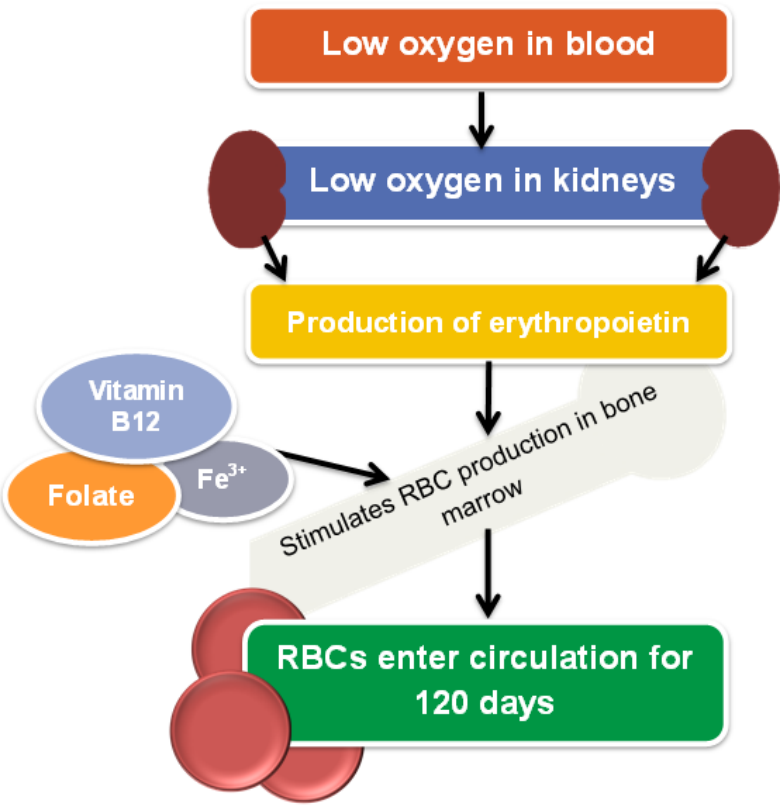
Pathophysiology (mechanism of disease)

The process of RBC production is called erythropoiesis.

When blood oxygen is low, this causes tissues to become hypoxic.
When the kidneys become hypoxic they release a substance called erythropoietin into circulation.
The erythropoietin stimulates RBC production in the bone marrow:

- this involves undifferentiated hematopoietic stem cells in the bone marrow to differentiate into RBCs
- vitamin B12 and folate are key nutrients in this process; it is thought that they are involved in the process of DNA synthesis in the new RBCs
- Fe^{3+} is the form of iron that is used in the production of haemoglobin that is found in RBCs. It is transported to the bone marrow by a protein called ferritin.[27]



When RBCs are matured, they pass into circulation where they last for 120 days. After this time they break down, the iron component is recycled and there are other waste products that are processed by the liver and excreted in the bile and urine. In adults 200 billion old erythrocytes break down and are replaced every day.[27]

Anaemia occurs when this process is disrupted. This may be due to, for example, reduced erythropoietin production (likely to be caused by chronic kidney disease), low vitamin B12, folate, or iron levels, or disruption of their transport into the bone marrow. There may also be issues with damage to the circulating RBCs.

For a deeper insight into the roles of folate, vitamin B12 and iron in erythropoiesis, access the following ScienceDirect topics **Erythropoiesis - an overview.**
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Diagnosis/detection

The diagnosis of anaemia is based on clinical history and the presence of symptoms. If anaemia is suspected, diagnosis can be aided by blood tests including full blood count, and depending on suspected cause, ferritin, vitamin B12 and/or folate levels. Other blood tests may be undertaken to help identify any underlying causes.

All unexplained anaemia or lack of response to treatment should be further investigated and may need urgent referral.[28,29]

The Welsh Centre for Pharmacy Professional Education (WCPPE) ***Biochemistry: Section 1*** e-learning aims to provide learners with a basic awareness of important blood tests and how to interpret them to support the diagnosis and management of patients. *Section 1* covers full blood count, inflammatory markers and coagulation. Access this programme to learn more about the diagnosis of different types of anaemias.

Northern Ireland Transfusion Committee has produced ***Investigation and management of the adult patient with anaemia (2015)*** which outlines how blood test results may be used to guide diagnosis and management.

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Treatment

In all types of anaemia the underlying cause should be addressed if this is an option.

Iron deficiency

Access ***Anaemia – iron deficiency, Scenario: Management*** for information on the treatment options in iron deficiency anaemia.

Vitamin B12 and folate deficiency

Access ***Anaemia – B12 and folate deficiency, Scenario: Management*** for information on the treatment options in B12 and folate deficiency anaemia.

Aplastic anaemia

In aplastic anaemia blood transfusion may improve quality of life, and there are also specialist pharmacological therapies available along with stem cell transplant.[30] Patients with mild symptoms require little or no therapy[31], whereas others may have life-threatening pancytopenia (low RBC, WBC and platelets). This will need to be treated as a medical emergency.

Haemolytic anaemia

When a diagnosis of haemolytic anaemia is made, a specialist referral is normally undertaken. If symptomatic, people may need an infusion. Folic acid may be prescribed for those who have a high reticulocyte (immature RBC) count due to it being rapidly depleted when there is high red cell production. Certain types of haemolytic anaemia may respond to treatments such as corticosteroids, monoclonal antibodies and intravenous immunoglobulins.[14]

Anaemia of chronic diseases

The treatment of anaemia of chronic disease depends on the underlying condition. Iron supplementation is recommended when iron deficiency is present. There may be occasions when RBC transfusion is offered. RBC transfusion is avoided in cancer and chronic kidney disease (CKD). An alternative option is erythropoietin analogues such as darbepoetin alfa.[15]

For more information about the treatment of anaemia in CKD and the use of erythropoietin analogues, visit NICE guidance ***Chronic kidney disease: assessment and management*** **[NG203].**

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Patient support

The NHS offers the following pages:

- ***Vitamin B12 or folate deficiency anaemia***
- ***Iron deficiency anaemia***
- ***Sickle cell anaemia: Pamela's story***

The ***B12 Deficiency Support Group*** is a charity which aims to raise awareness of vitamin B12 deficiency and offer information and support to those affected by it.

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Further resources

National guidance

British Society of Gastroenterology's ***Guidelines for the management of iron deficiency anaemia***.

The Renal Association's ***Clinical Practice Guidance Anaemia of Chronic Kidney Disease***, 2017, updated 2020 and available on the UK Kidney Association website.

British Journal of Haematology's ***Guidelines for the diagnosis and treatment of cobalamin and folate disorders***.

NICE Treatment Summary - **Anaemias**

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External websites

CPPE is not responsible for the content of any non-CPPE websites mentioned on this page or for the accuracy of any information to be found there.

All web links were accessed on 21 March 2022.

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References

1. World Health Organization. ***Anaemia***. No date.
2. World Health Organization. ***Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity***. 2011.
3. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – iron deficiency. Definition***. November 2021.
4. Lab Tests Online UK. ***Anaemia***. January 2021.
5. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – B12 and folate deficiency. Definition.*** July 2020.
6. NHS. ***Vitamin B12 or folate deficiency anaemia. Causes***. May 2019.
7. Patient. ***Anaemia of chronic disease***. November 2016.
8. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – iron deficiency. Prevalence.*** November 2021.

9. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – B12 and folate deficiency. Prevalence***. July 2020.
10. BMJ Best Practice. ***Aplastic anaemia in adults. Epidemiology***. August 2018.
11. BMJ Best Practice. ***Haemolytic anaemia. Epidemiology***. March 2018.
12. BMJ Best Practice. ***Anaemia of chronic disease. Epidemiology.*** July 2018.
13. NHS. ***Vitamin B12 or folate deficiency anaemia. Symptoms***. May 2019.
14. BMJ Best Practice. ***Haemolytic anaemia. Approach***. March 2018.
15. BMJ Best Practice. ***Anaemia of chronic disease. Approach***. July 2018.
16. NHS. ***Iron deficiency anaemia***. January 2018.
17. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – iron deficiency. Signs and symptoms.*** November 2021.
18. BMJ Best Practice. ***Aplastic anaemia in adults. Approach***. August 2018.
19. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – B12 and folate deficiency. Signs and symptoms***. July 2020.
20. University of California San Francisco. ***Hemoglobin and functions of iron***. No date.
21. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – iron deficiency. Causes***. November 2021.
22. Pernicious Anaemia Society. ***What is pernicious anaemia?*** No date.
23. NHS. ***B vitamins and folic acid***. March 2017.
24. BMJ Best Practice. ***Aplastic anaemia in adults. Aetiology***. August 2018.
25. Weiss G, Goodnough L T. **Anemia of chronic disease**. *New England Journal of Medicine.* 2005; 352:1011-1023.
26. BMJ Best Practice. ***Anaemia of chronic disease. Aetiology***. July 2018.
27. Koury M J, Ponka P. **New insights into erythropoiesis: The roles of folate, vitamin B12, and iron**. *Annual Review of Nutrition.* 2004; 24:105-131.
28. Northern Ireland Transfusion Committee. ***Investigation and management of the adult patient with anaemia: Microcytic anaemia***. August 2015.
29. National Institute for Health and Care Excellence. Clinical knowledge summary. ***Anaemia – iron deficiency. Management***. November 2021.
30. Killick S B, Bown N, Cavenagh J, et al. **Guidelines for the diagnosis and management of adult aplastic anaemia.** *British Journal of Haematology.* 2015; 172(2):187-207.
31. Patient Info. **Aplastic Anaemia**. [Internet]. May 2020.

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