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Vitamin B12 deficiency and pernicious anaemia

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What is vitamin B12 deficiency?

Vitamin B12 is essential for life. It is needed to make new cells in the body, such as the many new red blood cells which are made every day. Vitamin B12 is found in meat, fish, eggs and milk - but not in fruit or vegetables. A normal balanced diet contains enough vitamin B12. A lack of vitamin B12 leads to anaemia and sometimes to other problems.

Vitamin B12 deficiency symptoms

Symptoms due to anaemia

These are caused by the reduced amount of oxygen in the body.

- Common symptoms include tiredness, lethargy, feeling faint and becoming breathless.
- Less common symptoms include headaches, a 'thumping heart' (palpitations), altered taste, loss of appetite, and ringing in the ears (tinnitus).
- You may look pale.

Other symptoms

Cells in other parts of the body may be affected if you lack vitamin B12. Other symptoms that may occur include a sore mouth and tongue.

If left untreated, problems with nerves and psychological problems can develop. Psychological problems may include depression, confusion, and difficulty with memory, or even dementia. Nerve problems may include numbness, pins and needles, vision changes and unsteadiness.

What are causes of vitamin B12 deficiency?

Pernicious anaemia

Normally, when you eat foods with vitamin B12, the vitamin combines with a protein called intrinsic factor in the stomach. The combined vitamin B12/intrinsic factor is then absorbed into the body further down the gut at the end of the small intestine. (Intrinsic factor is made by cells in the lining of the stomach and is needed for vitamin B12 to be absorbed.)

Pernicious anaemia is the most common cause of B12 deficiency in the UK. It is classed as an autoimmune disease. The immune system normally makes antibodies to attack bacteria, viruses and other germs.

If you have an autoimmune disease, the immune system makes antibodies against certain tissues of your body. If you have pernicious anaemia, antibodies are formed against your intrinsic factor, or against the cells in your stomach which make intrinsic factor.

This stops intrinsic factor from attaching to vitamin B12 and so the vitamin cannot be absorbed into your body. It is thought that something triggers the immune system to make antibodies against intrinsic factor. The trigger is not known.

Pernicious anaemia usually develops over the age of 50. Women are more commonly affected than men and it tends to run in families. It occurs more commonly in people who have other autoimmune diseases. For example, thyroid diseases, Addison's disease and vitiligo (a condition where white patches develop on skin). The antibodies which cause pernicious anaemia can be detected by a blood test to confirm the diagnosis.

Stomach or gut problems

Various problems of the stomach or gut can be a cause of vitamin B12 deficiency. They are all uncommon causes. They include:

- Surgery to remove the stomach or the end of the small intestine. This
 will mean absorption of vitamin B12 may not be possible.
- Some diseases that affect the end of the small intestine where vitamin B12 is absorbed may affect the absorption of the vitamin - for example, Crohn's disease.
- Some conditions of the stomach may affect the production of intrinsic factor which is needed to combine with vitamin B12 to be absorbed - for example, atrophic gastritis (where the lining of the stomach is thinned).

Medicines

Certain medicines used for other conditions may affect the absorbtion of vitamin B12. The most common example is metformin which is a medicine often used for diabetes. Other medicines include colchicine, neomycin and some anticonvulsants used to treat epilepsy.

Note: long-term use of medicines that affect stomach acid production, such as H and proton pump inhibitors, can worsen vitamin B12 deficiency. This is because stomach acid is needed to release vitamin B12 bound to proteins in the food you eat. However, such medicines are not causes of vitamin B12 deficiency.

Dietary causes

It is unusual to lack vitamin B12 if you eat a normal balanced diet. Strict vegans who consume no animal or dairy products may not eat enough vitamin B12. Some foods are fortified with vitamin B12 - for example, some soy products, some breakfast cereals and some breads.

How is vitamin B12 deficiency diagnosed?

The initial blood tests will include a full blood count (FBC) to see whether you are anaemic. The full blood count test will also include a level called the mean cell volume (MCV), which is raised with vitamin B12 deficiency but also in some other conditions.

The level of vitamin B12 can be measured by a blood test. However some people may have symptoms of vitamin B12 deficiency despite normal vitamin B12 blood test results, or may have low blood levels despite having no symptoms. Therefore the results of these blood test need to be interpreted together with your symptoms.

The commonly used blood test for vitamin B12 measures the total amount of vitamin B12 in your blood. This includes "active" forms of vitamin B12 that can be used by your body, as well as the "inactive" forms, which cannot be used.

Therefore, if a significant amount of the vitamin B12 in your blood is inactive, a blood test may show that you have normal vitamin B12 levels, even though you have vitamin B12 deficiency because of insufficient "active" vitamin B12. Blood tests that only measure the amount of vitamin B12 in your blood that is "active" are not yet widely available.

Further tests are then needed to find out the cause of the vitamin B12 deficiency. These further tests include blood tests for intrinsic factor antibodies and gastric parietal cell antibodies. These blood tests help to find out whether you have pernicious anaemia.

Vitamin B12 deficiency treatment

You will need vitamin B12 injections. The injections are usually given frequently at the start of treatment. This quickly builds up the body's store of vitamin B12. Vitamin B12 is stored in the liver. Once a store of vitamin B12 has built up, this can supply the body's needs for several months. An injection is then only usually needed every two to three months to top up the supply.

The recommended dose **if you do not have any nerve problems** caused by pernicious anaemia is initially an injection three times a week for two weeks and then one injection every three months.

The recommended dose **if you do have any nerve problems** caused by pernicious anaemia is initially an injection every other day until there is no further improvement in your symptoms, then one injection every two months.

There is a small group of people with vitamin B12 deficiency who report that their symptoms come back (recur) before the usual three-monthly treatment dose. Therefore, some people have injections more often than three-monthly. However, this is not common and is best discussed with your doctor.

If you have pernicious anaemia the injections are needed for life. Apart from the discomfort of having an injection, you should have no side-effects from the treatment. The injections are simply replacing a vitamin that you need.

If the cause of your lack of vitamin B12 is diet-related rather than due to pernicious anaemia then treatment may be different. That is, after the initial treatment with injections of vitamin B12, dietary supplements of vitamin B12 (cyanocobalamin tablets) may be advised instead of injections.

Alternatively, injections of vitamin B12 twice a year may be recommended.

Read more in the separate leaflet called Diets Suitable for People with Anaemia.

Follow-up

The symptoms of anaemia usually improve quickly once treatment has begun. You may be advised to have a blood test every year or so. This will check that the anaemia is being treated successfully. A blood test may also be done to see that your thyroid gland is working well. (Thyroid problems are more common in people with pernicious anaemia.)

Any psychological or nerve problems caused by vitamin B12 deficiency may take a long time to treat and may not fully resolve with treatment. Prolonged or severe vitamin B12 deficiency may therefore cause permanent brain or nerve damage.

If you have pernicious anaemia, you are about three times more likely to develop stomach cancer than someone without pernicious anaemia, even when the anaemia is treated. See a doctor soon if you develop any stomach symptoms such as regular indigestion or stomach pain.

Further reading

- Guidelines for the diagnosis and treatment of cobalamin and folate disorders; British Committee for Standards in Haematology (2014)
- Anaemia B12 and folate deficiency; NICE CKS, July 2020 (UK access only)
- Shipton MJ, Thachil J; Vitamin B12 deficiency A 21st century perspective. Clin Med (Lond). 2015 Apr;15(2):145-50. doi: 10.7861/clinmedicine.15-2-145.
- Marchi G, Busti F, Zidanes AL, et al; Cobalamin Deficiency in the Elderly. Mediterr J Hematol Infect Dis. 2020 Jul 1;12(1):e2020043. doi: 10.4084/MJHID.2020.043. eCollection 2020.

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Authored by:	Peer Reviewed by: Dr Laurence Knott	
Originally Published:	Next review date:	Document ID:
19/11/2023	16/02/2021	doc_4372

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