Vitamin B12 Deficiency

B12 deficiency is common: 6% of general population and 20% of those over 60 years.

CAUSES

Pernicious Anaemia

The commonest cause of B12 deficiency is **pernicious anaemia (PA).** This name is confusing as there is rarely any anaemia (this develops at a later stage if the disease is left untreated). **Pernicious anaemia is an auto-immune disease.** The reason it happens is because of atrophy (wasting away) of the parietal cells in the stomach or an antibody blocks the production of intrinsic factor. Normally parietal cells produce intrinsic factor which combines with B12 broken down from food in the stomach. Later this complex of intrinsic factor and B12 is absorbed in the terminal ileum (last part of small intestine). **The basic problem in pernicious anaemia is the body's inability to produce intrinsic factor.**

Drugs

Some drugs block the production of acid or intrinsic factor in the stomach and therefore produce B12 deficiency. Top of the list are proton pump inhibitors (PPIs) such as lansoprazole and omeprazole. The diabetic drug metformin can also block B12 absorption. Other acid-blockers such as ranitidine, plus anti-inflammatory drugs (such as ibuprofen), the pill and some epilepsy drugs can cause problems.

Diet

Vegetarians and vegans can develop B12 deficiency. However, it is quite difficult to do this as there is usually plenty of B12 in the diet, especially from meat, fish and diary. Even for vegetarians fortification of foodstuffs, like cereals, with B vitamins gives some protection. Oddly All-bran is particularly high in B12. Mushrooms, especially shiitake mushrooms are a good vegetarian source of B12. One of the main sources of B12 is from friendly bacteria in our gut but these can be damaged and reduced in number, notably after taking antibiotics.

Surgery

Stomach surgery (gastric by-pass) or surgery to the terminal ileum can cause B12 deficiency.

Pathogens

Rare causes are the fish tapeworm (diphyllobothrium latum) and the parasite, giardia lamblia. A clue to either of these is high eosinophils in the blood.

SYMPTOMS

B12 deficiency can cause a wide variety of symptoms but fatigue is the most common and neurological symptoms such as nerve damage are the most serious (this can happen if the disease is left untreated). In addition, brain fog, breathlessness, swollen cracked tongue, dry skin, premature greying, imbalance and weakness. Other symptoms and signs include brittle nails with ridges 49%, waking tired 36%, memory loss 68%, confusion 62%, burning feet and legs 35%, diarrhoea 70%, abdominal cramps 45%, indigestion 42%, irritable 80%, impotence 65%, mood swings 60%, Depression is also common, and psychosis can also occur.

DIAGNOSIS

Unfortunately, this is not straightforward. Nearly half of patients get misdiagnosed initially. The usual method is to **check the level of B12.** A level under 197 suggests deficiency and a level below 330 is suboptimal and could represent PA. **It is worrying that the B12 test can be normal in 22 to 35% of people with B12 deficiency.** The test is unreliable because the test measures two forms of B12: the inactive form, holohaptocorrin and the active form holotranscobalamin. As little as 10% of B12 can be in the active form. This means it is possible to have a deficiency of active B12 and for the test to be completely normal (if there is plenty of inactive B12 present). To complicate things further, PA patients can have high levels of intrinsic factor antibodies and this can falsely raise the level of B12.

It is possible to check the active part of B12 by means of the **holotranscobalamin** test but this is not available in most labs (although widely used in Europe and the USA). Another test, **methylmalonic acid (MMA),** is raised in B12 deficiency and gives a further guide. Again it is not available in many labs.

A further two tests are used in pernicious anaemia. These are **intrinsic factor antibodies** and **parietal cell antibodies**. If intrinsic factor antibodies are present this is **virtually diagnostic of pernicious anaemia** but unfortunately only 40 to 60% of patients with PA react positively to this test. The parietal cell antibodies are present in 80% of cases of PA sufferers but 10% of the normal population also have these antibodies so it is not diagnostic.

The bottom line is that it is possible to have pernicious anaemia with normal B12 levels and negative antibody tests. If the symptoms suggest B12 deficiency then a trial of B12 is sometimes needed.

TREATMENT

Treatment is normally by injections of B12 with hydroxocobalamin. However it is possible to use B12 tablets (cyanocobalamin). Even in PA a small fraction (1%) of B12 is absorbed at the terminal ileum without intrinsic factor. If a large enough quantity of B12 is present then enough can be absorbed. However absorption is unpredictable. Other forms of B12 deficiency can manage with tablets better so in these cases tablets may be best. However the preferred treatment for pernicious anaemia is with injections. *However even with injections there can be a problem. Hydroxocobalamin (from the injection) is converted to the active form, methylcobalamin. Unfortunately, some people cannot convert hydroxocobalamin to methylcobalamin and need methylcobalamin injections. However these are no longer available on the NHS.*

Normally, after diagnosis, 3 injections weekly are given for two weeks and then treatment is given 3 monthly. If there is nerve damage, treatment is given 3 times a week until improvement occurs.

However there is a problem with these guidelines. The amount of B12 that is needed varies markedly, probably for genetic reasons, and many PA sufferers need injections every month (monthly treatments are standard in the USA and many European countries and were the norm in the UK until 1974). **Basically many PA patients (possibly up to 80%) will need B12 injections more frequently than three monthly.**

A particular area of confusion is blood tests done after treatment. The only purpose of these is to show if the levels are low. A high level (some patients require levels as high as 2000, which is twice normal, to feel well) as it is virtually impossible to take too much B12 (The late Dr Patrick Kingsley who treated over 9000 patients with multiple sclerosis with a high degree of success often used 20,000micrograms daily). However sometimes B12 is mistakenly stopped by doctors and nurses worried by the high level – this can result in the illness relapsing. **PA patients need treatment for the rest of their life.**