



MANAGEMENT FILE

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MEA membership costs £18 a year for people living in the UK/BFPO.
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the ME association



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Vitamin B12 – could it be a safe and effective form of treatment?

INTRODUCTION

We receive regular queries and feedback relating to the use of vitamin B12 in ME/CFS. Vitamin B12 used to be prescribed by doctors as a 'tonic' for people with a variety of complaints, especially those involving fatigue. However, it is no longer used in this way due to the lack of any sound evidence that 'tonics' actually work.

So is there any evidence of vitamin B12 deficiency in ME/CFS? And could vitamin B12 be a safe and effective form of treatment for ME/CFS?

This Management File tells you all you need to know about vitamin B12.

WHAT IS VITAMIN B12?

Vitamin B12 is involved in energy production, tissue and cell repair, nerve health, and the production of red blood cells that carry oxygen around the body. So we all need a regular dietary supply, along with good intestinal absorption, of this vital vitamin.

WHICH ARE BEST DIETARY SOURCES OF VITAMIN B12?

Good dietary sources include meat, salmon, milk, eggs, some fortified breakfast cereals, yeast extract – including Marmite, and some soy products.

So a healthy balanced diet containing meat, poultry, seafood and dairy produce should be providing more than enough. The body stores several years

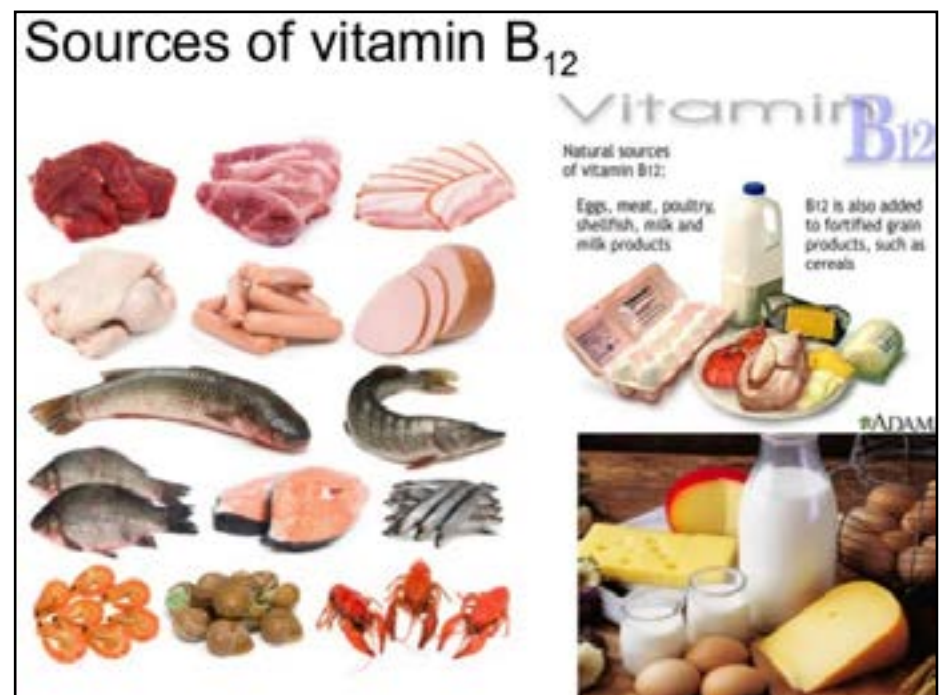
supply of vitamin B12 in the liver. Taking extra vitamin B12 in the form of over-the-counter supplements isn't therefore necessary or sensible – unless you are at increased risk or a deficiency of vitamin B12 has been identified.

WHAT ARE THE SYMPTOMS OF VITAMIN B12 DEFICIENCY?

As vitamin B12 is required for a wide range of body functions, it can cause an equally wide range of symptoms – some of which are related to nerve damage (neuropathy). These include several symptoms that can also occur in ME/CFS:

○ Fatigue and lack of energy

- Breathlessness
- Abnormal sensations/'pins and needles' sensations (paraesthesiae) or loss of sensation in the fingers or toes
- Muscle weakness or clumsiness in the hands or feet
- Problems with balance and/or walking
- Visual disturbances
- Problems with memory, concentration, judgment, even confusion
- Palpitations (due to the anaemia)
- Mood changes, including depression
- Tinnitus – hearing strange noises in the ears



Vitamin B12 deficiency should therefore form part of the clinical assessment and differential diagnosis of ME/CFS, especially in cases where there is no clear infective onset or where sensory neurological symptoms are present.

Other symptoms and signs are not characteristic of ME/CFS:

- Sore red tongue (= glossitis)
- Mouth ulcers
- Loss of appetite and weight
- Pale yellow tinge to the skin
- Subtle deterioration in eyesight

Long-term and more severe deficiency of vitamin B12 can lead to serious neurological complications, including spinal cord degeneration (causing severe weakness and poor co-ordination) and heart failure.

And it's important to note that neurological changes due to vitamin B12 deficiency may develop gradually in the absence of any clear changes in the blood picture.

WHAT CAUSES VITAMIN B12 DEFICIENCY?

There are several ways in which people can develop vitamin B12 deficiency:

First is a very important autoimmune disease called pernicious anaemia (PA). An autoimmune disease is where the body's immune system produces harmful antibodies (= autoantibodies) against its own tissues, and there is some evidence to indicate that ME/CFS has an autoimmune component.

In the case of PA, the immune system produces antibodies against healthy cells in the stomach where a molecule called intrinsic factor, which helps vitamin B12 to be absorbed in the small intestines, is produced.

Pernicious anaemia is the commonest cause of vitamin B12 deficiency in the UK. It is more common in women around the age of 60, especially when they have other autoimmune conditions.

Other causes include:

- **Diet** As food is the main source of vitamin B12, poor or restrictive diets – especially vegan diets lacking in meat, eggs and dairy produce – can cause vitamin B12 deficiency.
- **Intestinal diseases** such as Crohn's disease and coeliac disease – which can cause a decrease in absorption of vitamin B12 from the small intestine.
- **Stomach surgery** – where there is a loss of intrinsic factor-producing cells. Reduced stomach acid production, which is needed to separate B12 from protein in food.
- **Drugs** – including anticonvulsants, proton pump inhibitors for indigestion and metformin for type-2 diabetes. This is because some prescription-only drugs affect the way in which the body absorbs vitamin B12. Oestrogen containing oral contraceptives can reduce vitamin B12 levels – as can pregnancy.
- Functional vitamin B12 deficiency – where there is a problem with proteins that transport vitamin B12 between cells. This can also cause neurological complications.

Stores of vitamin B12 last a long time – several years – so it can take a long time for symptoms to appear and become obvious. It is also worth noting that vitamin B12 deficiency becomes more common as people grow older.

HOW IS VITAMIN B12 DEFICIENCY DIAGNOSED?

Vitamin B12 deficiency results in the bone marrow producing abnormal blood cells that are larger than normal – megaloblastic cells – and do not work as efficiently as normal red cells. The resulting anaemia is called a macrocytic anaemia.

A vitamin B12 blood test measures the total amount of vitamin B12 – active and inactive – in the serum (the liquid part of the blood). If a significant amount of vitamin B12 is inactive in the blood, this

can cause a misleadingly normal result.

So there is a weakness with the current blood test as it is not measuring the actual level of active B12 in the cells in the body. Second line tests, where use and availability are limited, include plasma methylmalonic acid and plasma homocysteine. Testing for intrinsic factor antibody can help to confirm the diagnosis.

The level of folate is also usually checked at the same time for the possibility of co-existent folate deficiency anaemia.

IS THERE ANY EVIDENCE OF VITAMIN B12 DEFICIENCY IN ME/CFS?

At present, there is no sound scientific evidence of vitamin B12 deficiency in ME/CFS.

IS THERE ANY EVIDENCE THAT VITAMIN B12 IS A SAFE AND EFFECTIVE TREATMENT FOR ME/CFS?

At present, there is no evidence of vitamin B12 deficiency in ME/CFS and no evidence from a good quality clinical trial to show that vitamin B12 is an effective form of treatment for ME/CFS.

However, Regland *et al* from Sweden have reported that in a survey of 38 ME/CFS patients who had been receiving vitamin B12 injections in combination with folic acid at least once a week for six months, 15 reported a good response and 23 reported a mild response.

Abstract: www.ncbi.nlm.nih.gov/pubmed/25902009

The MEA also receives regular feedback from people who feel that using vitamin B12 has been beneficial and there are also some doctors who believe it is effective. The MEA has therefore been discussing the possibility of funding a clinical trial that would assess the safety and efficacy of using vitamin B12 in ME/CFS.

Vitamin supplements are not recommended in the NICE guideline on ME/CFS. So most doctors are reluctant to prescribe vitamin B12 injections to people with ME/CFS – unless there are sound reasons for doing so.

Vitamin B12 injections do not normally produce any serious side-effects. Minor side-effects can include fever, headache, nausea and dizziness.

However, it is important to make sure that a diagnosis of PA has been excluded before self-treating with vitamin B12. This is because some symptoms of PA can overlap with ME/CFS. And if not properly treated, this could cause permanent and serious damage to the nerves in the spinal cord – a condition called sub acute combined degeneration of the spinal cord.

HOW IS VITAMIN B12 DEFICIENCY TREATED?

This will depend on the cause. If there is a lack of vitamin B12 in the diet, vitamin B12 tablets in conjunction with increasing the amount of good dietary sources of vitamin B12.

If there is a problem with intestinal absorption, as happens with PA, then vitamin B12 has to be given by an injection containing hydroxocobalamin – which is retained in the body longer than cyanocobalamin. Tablets or mixtures cannot be absorbed in the case of PA.

PA is a lifelong condition which can cause serious neurological problems if untreated or not properly treated. So treatment with injections has to be for life. After the initial course of treatment

the injections are then given every three months. If folate deficiency is also identified, folic acid tablets are prescribed.

FURTHER INFORMATION ON VITAMIN B12 AND PERNICIOUS ANAEMIA

- The following NHS guideline describes how people should be assessed and managed who have a blood test that indicates varying degrees of vitamin B12 deficiency: <http://tinyurl.com/o7a35aa>
- For information about lab tests for Vitamin B12 <http://tinyurl.com/hnu9vv6>
- For information about pernicious anaemia and sub-acute combined degeneration of the spinal cord: <http://tinyurl.com/zx7pmbw>
- NICE do not recommend the use of vitamin B12 in ME/CFS, or as a treatment for undiagnosed fatigue. This has led to disciplinary action by the GMC: <http://tinyurl.com/on8wltx>
- To contact the Pernicious Anaemia Society: <https://tinyurl.com/y2sd9fg6>
- For information about the myths associated with Vitamin B12: <https://tinyurl.com/y5aaw4l7>



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