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Diagnostic testing for B12 deficiency & Pernicious Anaemia

If you think you may have a B12 deficiency, you should have the following tests done.

Serum B12 - reference range varies from lab to lab. The article below suggests the reference range for B12 should be reconsidered: <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2011.02485.x/pdf>

Serum folate - (determines the amount of folate in the blood) this must be a **fasting test** because the result can be influenced by what you ate the night before. Folic acid should never be taken or prescribed unless B12 levels have been checked. Folate levels need to be kept in the high end of the reference range in order for the B12 to be properly utilised. RBC Folate is a better predictor see below.

RBC folate - (red blood cell folate - determines the amount of folate in storage in the cells). Folic acid should never be taken or prescribed unless B12 levels have been checked. Folate levels need to be kept in the high end of the reference range in order for the B12 to be properly utilised. The RBC folate test is best to have because it can predict a potential folate deficiency before it may show in a serum folate test. Low folate increases loss of B12:
<http://link.springer.com/article/10.1007%2FBF00256639>

Low folate also falsely increases B12 levels. If your folate level is low, this prevents a lot of the B12 being converted to methylcobalamin and adenosylcobalamin (the active B12 in the body). This in turn causes the B12 analogues (inactive B12) to increase and the cobalamin (active B12) to decrease. The serum B12 test cannot distinguish between active B12 and inactive B12 so the B12 analogues are included in the serum B12 test.
<http://www.ncbi.nlm.nih.gov/pubmed/7221475>

Ferritin - (iron storage) level should be at least 80 to 100. Ferritin levels must be monitored because B12 injections increase the production of red blood cells which, in turn, places a demand on iron stores. It is important to correct any signs of iron deficiency:
<http://haematologica.com/content/91/11/1506.full.pdf>

In addition to the above, a complete blood count should be done (see end of document).

Further diagnostic testing - for those who are symptomatic, but in the grey zone for serum B12

If you have access to the . . .

MMA - (methylmalonic Acid), **uMMA** and **Homocysteine** tests, they should be done. The link below explains the MMA test:
<http://www.b12.com/>

Low B12 and low folate will increase the MMA level. Low B12, low folate and low B6 will increase homocysteine levels. A high Homocysteine level will cause a build up of plaque in the arteries and lead to heart disease. MMA and homocysteine tests should be done to rule out a functional B12 deficiency. Many times your B12 level will fall within the normal range of the reference scale. However, an elevated MMA and homocysteine result means you are B12 deficient and possibly folate deficient. The article below is an excellent explanation of homocysteine:
http://www.lef.org/protocols/heart_circulatory/homocysteine_reduction_01.htm



Homocysteine - levels should be checked because of Factor V Leiden disorder which is an inherited blood-clotting disorder that increases the risk of venous thrombosis. Low B12 and low folate levels are a factor in increasing homocysteine levels:

<http://www.ncbi.nlm.nih.gov/pubmed/14580166>

The article below is a research article on functional B12 deficiency and how the holotc (Active B12) and MMA test can determine between B12 depletion and a functional B12 deficiency:

<http://www.ncbi.nlm.nih.gov/pubmed/14656029>

If your doctor will only do a complete blood count, serum B12 and folate and if you are told you do not have a B12 deficiency, then ask for a referral for the Active B12 test which is available in the UK now, in some parts of the United States and will soon be available in Canada. An explanation of the test:

The Active B12 test differs from the serum B12 test because it can determine those cobalamins which are active (methylcobalamin and adenosylcobalamin) and those which are inactive (B12 analogues).

Axis Shield developed the Active B12 test..the link below from their website explains the test:

<http://www.active-b12.com/What-Is-Active-B12>

Pernicious Anaemia

If you are diagnosed with B12 deficiency and want to know if you have pernicious anaemia, ask for the following tests:

Gastric Intrinsic Factor Antibodies – if you test positive for antibodies, this confirms a diagnosis of pernicious anaemia. However, a negative result does not mean you do not have pernicious anaemia, it could mean you fall within the 40 per cent of PA patients who have PA but do not carry the antibody. There are other causes of B12 deficiency. A family history of pernicious anaemia increases the chance of having intrinsic factor antibodies. Note: you need 72 hours clearance of **any** B12 before taking the test.

Gastric Parietal Cells Antibodies – they are not as sensitive for pernicious anaemia as intrinsic factor antibodies because gastric parietal cell antibodies are found in patients with diabetes and thyroidism. However, if you have a low B12 and are positive for gastric Parietal Cells Antibodies, most doctors will diagnose you with PA.

The link below gives a good explanation of IFA and PCA, scroll partway down the page:

<http://www.allergy.org.au/health-professionals/papers/consensus-on-anti-intrinsic-factor-antibody-testing>

Serum gastrin – must be a fasting test. It can determine if there is an excess production of gastrin and gastric acid. Pernicious anaemia causes a reduction of acid in the stomach. The stomach will compensate by trying to increase acid..an elevated serum gastrin test result likely means your stomach has low acid. An accompanying gastric PH level test should also be done.

The Schilling test was used to diagnose PA until about 2010 when it was discontinued. The test investigated why you couldn't absorb B12 and involved four different stages. It could determine why you couldn't absorb B12, either because of intrinsic factor antibodies or small bowel overgrowth. To date there is no test that has been able to replace this test, explanation below:

<http://www.nlm.nih.gov/medlineplus/ency/article/003572.htm>



There is a close association between thyroidism and PA/B12 deficiency. For that reason thyroid levels should be checked yearly. In addition to TSH (thyroid Stimulating Hormone), a good doctor will also order Free T4, Free T3 and thyroid antibodies. These tests will certainly show if you have a thyroid problem or a potential thyroid problem. Unfortunately, most doctors will just order a TSH test.

The reference range for TSH varies from country to country. Most thyroid forums say the upper level for TSH should be 3 and not 5. The range is 0.5 – 5.0. Note, when you are hypothyroid (low in thyroxine production) your TSH level goes high..so you could have a result of above 5. However, when Free T4 and Free T3 levels are checked, you would be low in them. Keep in mind that in hypothyroid patients, the TSH is high whereas in Hyperthyroid patients the TSH is low but the Free T4 and Free T3 would be high. For more information visit - <http://www.thyroiduk.org.uk>.

A complete blood count that will include a haematology report (RBC Indices) will help to determine a B12 deficiency.

Tests included in a haematology report are;

MCV (Mean Corpuscular Volume) Reference range is usually 80 – 100 (Note, I will not use units unless necessary). This reference range was changed about 7 to 10 years ago, the range used to be 80 – 94. Older research suggests that anyone with an MCV above 94 should be checked for B12/folate deficiency. Other health disorders such as diabetes and thyroidism can also elevate the MCV level. In short, B12 deficiency/folate deficiency increases MCV. However, iron deficiency decreases the MCV so if you are B12 deficient and iron deficient, this will balance out the MCV so that it will give a normal result. If your MCV goes below 87, then you need to make sure your doctor checks Ferritin levels.

MCH - Mean Corpuscular Haemoglobin – mirrors MCV..if your level is above normal or on the high end, then this is suspicious for B12 deficiency or folate deficiency or both. If it is on the low end, this would indicate a potential iron deficiency.

MCHC - mean corpuscular haemoglobin concentration also mirrors MCV and MCH when an anaemia is present, if it sits towards the high end, this is indicative of B12 or folate deficiency, if it sits towards the the low end, this is indicative of an iron deficiency. The ferritin level would be a good indicator here if you are developing an iron deficiency.

RDW - Red cell distribution width – range is 11 to 15 % although this can vary from lab to lab, the test calculates any change in size of the red blood cells. Along with the MCV, the RDW result if high, usually means a B12/folate deficiency. However, this is not true if there is an iron deficiency because iron deficiency will also increase the RDW.

WBC - white blood cells – it is found most PA patients tend to be on the low normal end of the reference range because of autoimmune conditions.

Remember to always get copies of your test results. You are entitled to them and this is very important. Never accept your doctor's answer that your result is ok or normal. You could be on the low end of normal of the reference range which would not help you at all.

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