

NHS FORTH VALLEY

B12 and Folate: A Practical Guide

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Consultation and Change Record

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<p>Consultation Process:</p>	<p>This guide was written with significant input from Drs Neilson and Brammer Consultant Haematologists and drew heavily from the Laboratory Handbook.</p> <p>Dr G McLean Consultant in Old Age Psychiatry, Dr C Neumann, Consultant Neurologist and Dr P Bramley, Consultant Gastroenterologist also provided input and agreed the final version.</p> <p>Dr Leslie Cruickshank Prescribing Advisor was consulted.</p> <p>Pharmacy has also been consulted.</p>
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B12 AND FOLATE TESTING – A PRACTICAL GUIDE

TESTING	<p>Because of the close relationship in metabolism B12 and folate should be tested concurrently</p> <p>Indications for Testing</p> <ul style="list-style-type: none"> • Neuropsychiatric symptoms where cause is unknown • Macrocytosis – MCV>100 • Macrocytic Anaemia / Pancytopenia <p>Also consider testing in patients with:</p> <ul style="list-style-type: none"> • Previous gastric surgery including gastric banding • Inflammatory Bowel disease • Coeliac Disease • Vegetarian and Vegan diet • Diabetics taking Metformin • Gastric hypochlorhydria due to age related gastric atrophy or proton pump inhibitor
Caution	Neurological symptoms due to B12 deficiency can occur in the absence of FBC changes
Note	<p>B12 deficiency is less likely with an MCV of 100-110</p> <p>Consider other causes of raised MCV – check LFTs, TFTs, haemolysis.</p> <p>B12 testing is NOT required when a patient is on B12 replacement</p> <p>Non specific tiredness alone is NOT an indication for B12/folate testing.</p>
B12 RESULTS	<p>The clinical picture is the most important factor in assessing the significance of B12 and folate results. There is no “gold standard” test and no level that defines deficiency</p> <ul style="list-style-type: none"> • B12<120 is usually ABNORMAL. • B12 120-180 is BORDERLINE and the result needs to be interpreted in the clinical context. • B12>180 is usually NORMAL.
Caution	Rarely False normal B12 results are seen in patients with deficiency due to high levels of Intrinsic Factor Antibody. IF Ab should be checked when there is a STRONG clinical suspicion of B12 deficiency
Note	<p>Women taking oral contraceptives may show decreased blood vitamin B12 levels because of a decrease in cobalamin carrier protein, rather than a deficiency state</p> <p>Vitamin B12 levels may be falsely low in pregnant women because of the increased plasma volume of pregnancy rather than actual deficiency of vitamin B12. This makes it practically very difficult to diagnose vitamin B12 deficiency in pregnancy.</p>
MANAGEMENT OF B12 RESULTS	<p>B12 < 120: this is low</p> <ul style="list-style-type: none"> • Check Anti Intrinsic Factor antibodies PRIOR to treatment • Anti-IF antibodies are diagnostic of Pernicious Anaemia • Schilling tests are no longer available and anti gastric parietal cell antibodies are non specific and non diagnostic • Negative Anti-IF antibodies does not exclude Pernicious Anaemia and in the absence of history or examination findings suggestive of terminal ileal disease or another cause of B12 deficiency a presumptive diagnosis of Pernicious Anaemia can be made • The diagnosis of Pernicious Anaemia means that the patient will require lifelong treatment with parenteral B12 • Dietary deficiency can occasionally cause levels this low but only when the diet is deficient in B12 over a prolonged period such as in dementia or veganism. Take a dietary history. <p>B12 120 -180: this is a borderline result</p> <ul style="list-style-type: none"> • Check Anti-IF antibodies PRIOR to treatment • Anti-IF antibodies are diagnostic of Pernicious Anaemia • Otherwise management of B12 at these levels is dependent upon the clinical situation. • It is a normal finding in some patients • If no high clinical suspicion of B12 deficiency repeat level in 2 months. <ul style="list-style-type: none"> ○ If then normal no further tests required. ○ If remains low check IF antibody and if positive treat as for pernicious anaemia ○ If IF antibody negative consider trial of low dose oral B12 for 4 weeks and repeat level in 3 months ○ If level returns to normal consider causes of low level B12 and whether long term low dose oral B12 indicated

	<ul style="list-style-type: none"> ○ If level remains low consider treatment as IF antibody negative Pernicious Anaemia. • Use Clinical judgement depending upon the situation and consider discussion with Haematology . <p>Consider the patient's clinical situation: Examples</p> <ul style="list-style-type: none"> • Does the patient have myelopathy/peripheral neuropathy? Treat pragmatically with parenteral B12 • Does the patient have dementia? It is most likely that the deficiency is dietary and can be very severe depending upon the length of time the patient's diet has been sufficiently poor. Unless the patient has Pernicious Anaemia the aim is the return to a better nutritional status rather than defaulting to lifelong B12 injections. Low dose oral B12 can be considered. • Is the patient on long term proton pump inhibitors? Food-cobalamin malabsorption – Food bound B12 is poorly absorbed as it is not released from food usually due to reduced acid levels in stomach as a result of age or proton pump inhibitors. B12 in oral supplements is normally absorbed. • Is the patient anaemic with a macrocytosis? treat pragmatically with B12 and monitor response • Take a dietary history. Is the patient a vegan? Oral B12 replacement (SLS) may be needed. • Does the patient have symptoms suggestive of terminal ileal disease? These patients may require onward referral • Does the patient have other auto immune disorders or a strong family history of auto immune disorders? Check IF antibody <p>B12 >180: this is normal, no action required</p>
Caution	Rarely B12 levels can be normal in severe deficiency in the presence of high IF antibody titre. If high clinical suspicion of B12 check IF antibody
Note	A trial of B12 can be considered with monitoring of response. Woman taking the OCP or HRT may have a low serum B12 – a level of 120-180 does not need to be repeated unless there is clinical concern. IF antibody is positive in 50-70% of patients with Pernicious anaemia.

B12 TREATMENT	B12 replacement is with Hydroxycobalamin 1mg IM 6 doses over 2 weeks as loading followed by 1mg injection each 3 months. Patients presenting with neurological symptoms should receive alternate day 1mg IM hydroxycobalamin until there is no further improvement and then 2 monthly 1mg injections.
Caution	Allergy to hydroxycobalamin is rare. Cyanocobalamin can be considered as an alternative but cross-reactivity can occur.
Note	High dose oral B12 replacement is used to treat pernicious anaemia in some countries. Cochrane review suggests it is as effective as IM B12 replacement. Current UK guidelines do not recommend oral B12 replacement and high dose tablets are not available within the NHS. High dose oral B12 replacement could however be considered in patients unable to tolerate IM B12. Discuss with haematology. Low dose oral B12 (50-150mcg daily) is available in the NHS. This can be used where dietary deficiency or gastric hypochlorhydria resulting in food cobalamin malabsorption is considered. In patients presenting with anaemia potassium levels can fall when treatment is started. The clinical significance of this is unknown but oral supplements can be considered. In patients presenting with anaemia a reticulocyte response to treatment should be seen by 7-10 days. FBC should be checked at 8 weeks to ensure it has normalised.

FOLATE	Folate levels should be checked for the same indications as B12 Isolated folate deficiency is rare but most commonly seen with <ul style="list-style-type: none"> • Dietary deficiency – lack of green leafy veg • Alcoholism • Pregnancy • Increased requirements <ul style="list-style-type: none"> ○ Haemolytic anaemia ○ Exfoliating skin disorders • Haemodialysis • Small bowel disease <p>There is no defined serum folate level that indicates deficiency. A level of <3mcg/l is used as the risk of megaloblastic anaemia increases below this level. A level of <3mcg/l should therefore be taken as suggestive, rather than diagnostic, of deficiency. Treatment of anaemia due to folate deficiency is 5mg oral folic acid daily.</p>
Caution	Ensure B12 levels are normal before giving oral folic acid replacement alone because, if B12 deficient, folate replacement alone can precipitate sub-acute combined degeneration of the cord .
Note	Serum folate levels reflect recent dietary intake Red cell folate is no longer available in Forth Valley Oral folic acid replacement is usually only required for 4 months as the cause is often dietary and reversible with dietary advice.

Resources

- Haematology & Blood Transfusion Laboratory Handbook, Forth Valley.
- Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Library 2005.
- Vitamin B12 for cognition. Malouf R, Areosa Sastre A. Cochrane Library 2003
- NHS Clinical Knowledge Summaries Clinical topic - Anaemia - B12 and folate deficiency
- BNF March 2011

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