

Information for Clinicians

Primary Care

Vitamin B12 deficiency

Amendment History

Issue	Status	Date	Reason for Change	Authorised
1	Published	03/10/2024	New Guideline	J Price

Vitamin B12 testing

- The routine laboratory test is Total Vitamin B12. This test is low cost, has a fast turnaround time and is widely available.
- Total Vitamin B12 tests are poorly performing with poorly defined ranges, and serum B12 levels do not always correlate with intracellular B12 levels. There should be awareness that whilst this guideline follows NICE NG239 the advice is maybe not as absolute as some areas of medicine.
- Neurological symptoms and megaloblastic anaemia are more predictive of true deficiency compared to some of the symptoms and signs.
- There is substantial variation between Total Vitamin B12 methods, therefore local reference ranges must be used and NICE NG239 thresholds do not apply. The method used locally performs much lower than the NICE thresholds.
- Tests for Active B12 and Methyl Malonic Acid (MMA - functional marker of B12 deficiency) may also be available but are much more expensive, have longer turnaround times, and still have limitations.
- The clinical picture is the most important factor in assessing the significance of test results assessing B12 status because there is no 'gold standard' test to define deficiency.
- Pre-test probability is crucial; should have high suspicion prior to ordering the test.

When to test

Offer a test for Total Vitamin B12 to people who have:

- at least 1 common symptom or sign (box 1) **and**
- at least 1 common risk factor (box 2).

Box 1

Signs and Symptoms

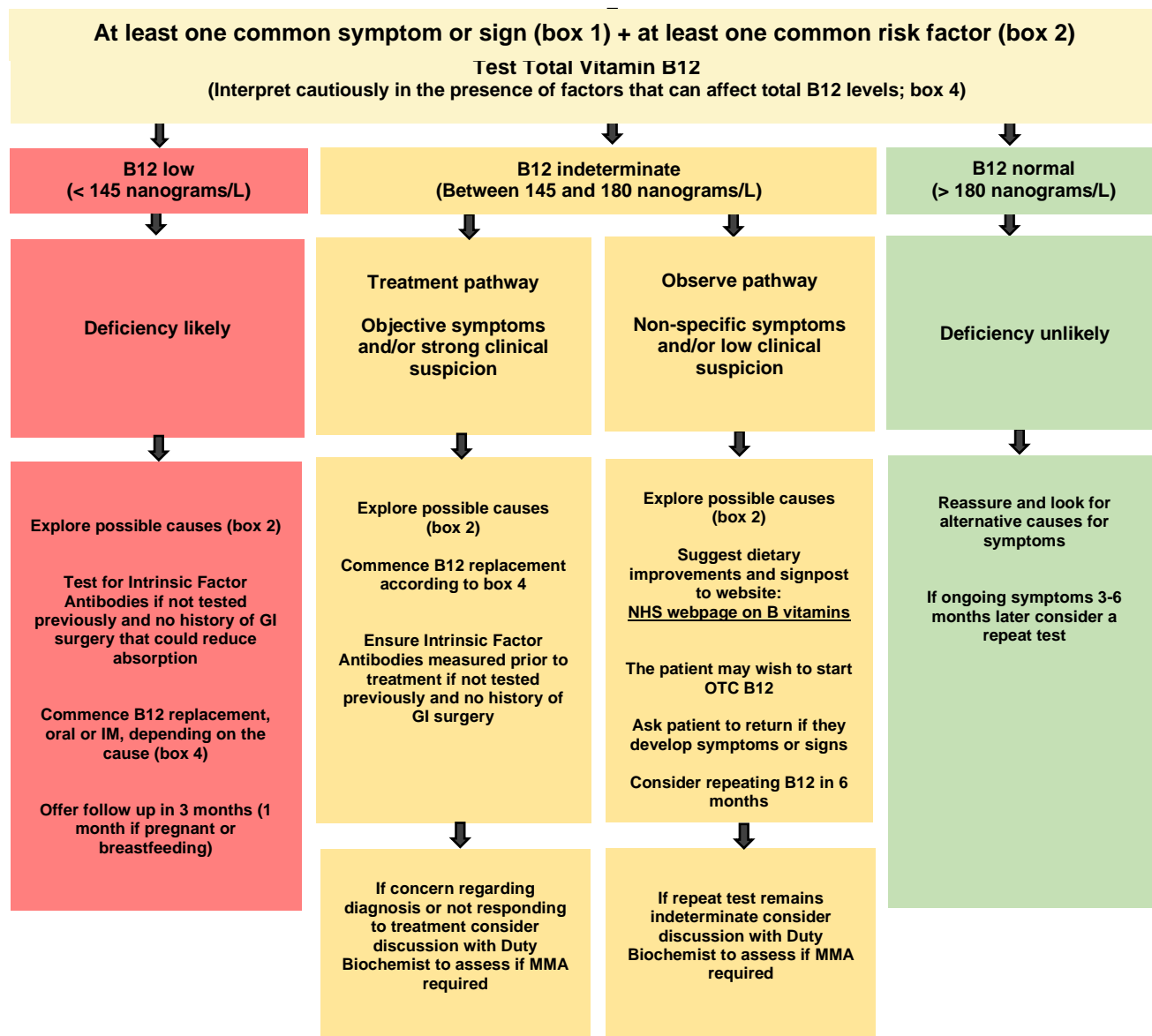
- FBC abnormalities** (anaemia / macrocytosis – *although these are not always present in B12 deficiency*)
- Cognitive difficulties** (difficulty concentrating / dementia symptoms/ brain fog)
- Eyesight problems** (blurred vision / optic atrophy / visual field loss)
- Glossitis**
- Neurological problems** (balance / gait problems / falls / pins and needles / peripheral neuropathy)
- Unexplained fatigue**
- Mental health issues** (anxiety, depression, psychosis)
- Symptoms or signs of anaemia that suggest iron treatment is not working properly during pregnancy or breastfeeding (measure Active B12 in pregnant people, see box 4)

Box 2

Risk factors

- Low B12 diet** (vegan / restricted diet / malnutrition)
- Malabsorption** (atrophic gastritis / coeliac disease)
- Previous gastrointestinal surgery** (bariatric / gastrectomy / terminal ileal resection)
- Previous radiotherapy** of the abdomen or pelvis
- Drugs** (colchicine / H2 receptor agonists / metformin / phenobarbital / pregabalin / primidone / PPIs / topiramate)
- Nitrous oxide** use
- Autoimmune disease** (thyroid disease / Sjogrens / T1DM)
- Family history** of B12 deficiency or autoimmune conditions

Vitamin B12 deficiency: interpreting results and replacement therapy



Box 3 Further investigations

- Intrinsic factor antibodies are required on all patients when B12 < 145 ng/L, persistent indeterminate results after 6 months or after a high Methyl Malonic Acid (MMA) result.
- Isolated low Ferritin is not a reason to test intrinsic factor antibodies
- MMA is an expensive test that needs to be sent to a referral lab
- MMA has **not been commissioned** therefore is only available when essential to the differential diagnosis and/or where a trial of supplementation is not adequate. Local Haem advise replacement of B12 and to monitor MCV
- **All MMA requests must be discussed with the Duty Biochemist in advance**
- If MMA confirms deficiency then IFA should be tested if not already done so and treatment should be initiated according to box 3

Box 4 Replacement

Start IM 1mg Hydroxycobalamin replacement in cases of B12 deficiency caused by:

- Previous gastro surgery or pernicious anaemia (3 monthly IM B12; lifelong, adjust frequency if clinically required)
- Malabsorption (treat until the cause is corrected)
- Nitrous Oxide use (review replacement if NO stopped)
- Pregnant or breastfeeding (stop after pregnancy and breastfeeding)
- Medicine induced causes sometimes require IM replacement; check the BNF (can stop once medication is stopped)
- If symptoms are not improving on maximum oral dose

For all other causes, start with oral replacement:

- Cyanocobalamin 50mcg daily is an adequate OTC dose, but when prescribing on FP10 1mg Orobalin od should be used.
- If symptoms are not improving on oral maximum dose, consider switching to IM replacement

Do not delay vitamin B12 replacement for people with megaloblastic anaemia or neurological symptoms, especially symptoms related to sub-acute combined degeneration of the spinal cord.

GP population differs from secondary care cohort; a larger proportion of indeterminate results may be normal or due to dietary restrictions; they can be given OTC B12 and followed up in 6 months.

Box 5 Problems with B12 measurement

- When offering a B12 test, ask the person if they are already using an over-the-counter preparation that contains vitamin B12 as this can influence the test results (false negative) without correcting the deficiency.
- Combined oral contraceptive pill can lower total B12 concentrations without causing a deficiency due to lower levels of carrier protein but deficiency may still be present (wash-out period is 6 weeks).
- Be aware that people of Black ethnicity may have a higher reference range for vitamin B12 than people of White or Asian ethnicity; therefore Black people may have deficiency at higher blood levels of B12.
- If pregnant, measure Active B12 as the first line test as this is thought to be more accurate in pregnancy. Refer to lab report for reference intervals; treatment is the same as above for low, indeterminate and normal levels.
- If suspected Nitrous Oxide use, measure MMA as the first line test as Total and Active B12 levels may be normal. Do not delay treatment waiting for result if haematological or neurological symptoms are present.
- If autoimmune gastritis (Pernicious anaemia) is still suspected despite a negative intrinsic factor antibody consider anti-gastric parietal cell antibodies, gastrin (specialist collection requirements), CobiSorb test, gastroscopy/biopsy.

Vitamin B12 deficiency: treatment follow up

