



Vitamin B12 deficiency in non-pregnant adults.

South Yorkshire Guideline on the Causes, Treatment and Management of Serum vitamin B12 deficiency in primary care.

Version 1

This document has been produced by Dr Sophie Holden and Melissa Goodlad for South Yorkshire by adapting the Sheffield Guideline Vitamin B12 Deficiency in Non-Pregnant Adults.

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Vitamin B12 Deficiency in Non-Pregnant Adults

Main Causes of B12 deficiency

- **Pernicious anaemia** (Autoimmune gastritis).
- **Dietary**; inadequate intake (e.g. vegan).
- **Medicines**; e.g. [metformin](#), H2-receptor antagonists & PPIs, colchicine, anticonvulsants (pregabalin, primidone, phenobarbital, topiramate), neomycin.
- **Malabsorption**: Gastrectomy, ileal resection, Coeliac, Crohn's, bariatric surgery.
- **Recreational nitrous oxide use**; N₂O oxidises B12 rather than destroying it, so vitamin B12 levels may be normal, but functionally inactive.

Patients presenting with neurological abnormalities/subacute combined degeneration of the cord require emergency assessment, treatment & investigations for B12 deficiency.

Subacute combined degeneration of the spinal cord commonly presents with sensory deficits, paraesthesia, weakness, ataxia, and gait disturbances.

It is also important to note that:

- Patients on the **oral contraceptive pill/HRT** may show decreased B12 levels due to decreased cobalamin carrier protein, rather than a deficiency state.

Reasons to Measure B12:

- ↑MCV*, anaemia, cytopenia.
- Clinical symptoms e.g. peripheral neuropathy, ataxia, paraesthesia, impaired gait, glossitis, blurred vision, scotoma, 'brain fog', unexplained fatigue.
- Risk factors for B12 deficiency.
- Folate deficiency.

*↑MCV is not specific for B12 deficiency. Other causes include alcohol excess, anti-neoplastic drugs & myelodysplasia.

*↑MCV may be absent in B12 deficiency.

Suggested Referral Pathways

- SDEC (Same Day Emergency Care) if suspected nitrous oxide toxicity.
- Neurology: D/w neurology on-call if suspected subacute combined degeneration of the cord or neurological symptoms, or if the diagnosis is unclear.
- Haematology if the cause is uncertain following investigations, or suspected cause is haematological malignancy (urgently refer) or other blood disorder.
- Gastroenterology if malabsorption is suspected or if there is a suspicion of gastric cancer.

Borderline B12 level (Indeterminate) * the term borderline/indeterminate is stated as numerical laboratory data may across South Yorkshire.

- Consider vitamin B12 replacement for people who have an initial test result that is indeterminate (low normal level) and meet any of the following criteria:
 - i. they have signs or symptoms that may deteriorate rapidly and have a major effect on quality of life (e.g. megaloblastic anaemia, cytopenia or neurological symptoms).
 - ii. they have a condition or suspected condition that is an [irreversible cause](#) of vitamin B12 deficiency (e.g. [autoimmune gastritis](#)).
 - iii. they have had surgery that can cause vitamin B12 deficiency (e.g. gastrectomy, terminal ileal resection or some types of bariatric surgery).
- Advise people with no symptoms or signs of vitamin B12 deficiency and an indeterminate B12 result to seek medical help if they develop symptoms or signs of deficiency.
- NB People already taking OTC vitamin B12 may have an increased B12 result without fully treating the deficiency; consider when interpreting results.

Treatment B12 Deficiency pathway *the term deficiency is stated as numerical laboratory data may across South Yorkshire.

- Check TFTs.
 - Check folate. If also folate deficient give B12 replacement first, 24 hours before folate replacement to protect neurones.
 - For people with confirmed vitamin B12 deficiency, consider an anti-intrinsic factor antibody (IFA) test if autoimmune gastritis is suspected and they have **not** previously had:
 - A positive anti-IFA test at any time, or
 - An operation that could affect vitamin B12 absorption (such as total gastrectomy or complete terminal ileal resection).
 - Also consider checking for serum anti-IFA if strong clinical features of B12 deficiency, such as megaloblastic anaemia or subacute combined degeneration of the cord, despite a normal B12.
- NB About **50%** with autoimmune gastritis (pernicious anaemia) will have IFA. If IFA is present, autoimmune gastritis is very likely, but its absence does not rule out a diagnosis.
- Offer serological testing for coeliac disease where the cause of vitamin B12 deficiency is still unknown.

Management of B12 Deficiency in Primary Care

Do not delay B12 replacement whilst waiting for test results in suspected megaloblastic anaemia and neurological symptoms, especially those related to subacute combined degeneration of the cord (including patients abusing nitrous oxide).

Do **not** give oral B12 replacement if IFA positive or high suspicion of autoimmune gastritis (pernicious anaemia).

NB. Patients presenting with severe anaemia may develop a transient hypokalaemia following treatment.

B12 REPLACEMENT	INITIAL TREATMENT	MAINTENANCE	COMMENTS
WITH neurological involvement	Initially IM hydroxocobalamin 1mg once daily on alternate days until no further improvement	IM hydroxocobalamin 1mg every 2 months	<i>Patient should be under specialist follow up. Symptoms may take up to 3 months to improve.</i>
WITHOUT neurological involvement:			
Autoimmune gastritis (Pernicious anaemia) or Malabsorption-induced:	Initially IM hydroxocobalamin 1 mg 3 times a week for 2 weeks	IM hydroxocobalamin 1mg every 3 months or oral cyanocobalamin 1mg daily	<i>Further testing of B12 is not required in those on regular IM replacement</i>
Medicine-induced	Either IM hydroxocobalamin 1 mg 3 times a week for 2 weeks Or oral cyanocobalamin 1mg daily	IM hydroxocobalamin 1mg every 3 months or oral cyanocobalamin 50micrograms one tablet daily taken between meals. *	<i>Review the use of the medication causing B12 deficiency to see if it is still needed or can be changed. Stop B12 replacement when medication stopped.</i> * If symptoms do not improve after 3 months, increase dose every 3 months in 50microgram steps up to 150microgram daily.
Deficiency of unknown cause	Initially IM hydroxocobalamin 1 mg 3 times a week for 2 weeks	Either continue IM hydroxocobalamin 1mg every 3 months OR oral cyanocobalamin 1mg daily*	<i>*based on clinical judgement and the person's preference</i>
Diet related	First line Dietary advice e.g. meat, salmon and cod, dairy, eggs, fortified foods (yeast products, breakfast cereals, soy products)		<i>In vegans, treatment may need to be lifelong. In other dietary causes treatment can be stopped once B12 is corrected and diet has improved. Further information can be found via the NHS website or the vegetarian society website</i>
	Second line. Advise to purchase over the counter (OTC) oral B12 or IM* hydroxocobalamin	Oral B12 50-150cmg daily.	<i>Advise to patient to purchase oral B12 OTC *IM hydroxocobalamin only if serious concerns about adherence or if person's clinical condition may deteriorate</i>

References: 1. [Anaemia - B12 and folate deficiency | Health topics A to Z | CKS | NICE](#) (last accessed June 2025) 2. [Overview | Vitamin B12 deficiency in over 16s: diagnosis and management | Guidance | NICE](#) (March 2024) 3. [Wolffenbuttel BHR et al. Vitamin B12. BMJ 2023; 383.](#) 4. [Devalia V et al. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. Br J Haematol. 2014; 166: 496-513](#) 5. [BNF \(British National Formulary\) | NICE](#)

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