

Vitamin B12 (cyanocobalamin) Measurement in Primary Care

Who should have a B12 measurement done?

How should we interpret the results?

What conditions should we think about when faced with a low B12?

What further investigations may be required if we find a low B12?

How should we treat a low B12?

Basics

Needed for DNA synthesis

Animal products only source, esp liver

Diet produces 5 - 7 μg per day (close to minimum requirement)

Stores in healthy = 2 - 5 mg so that deficiency takes years to develop

Dietary B12 is protein bound and released by acid pepsin

Binds to R factor in saliva and gastric juice

Pancreatic protease cleaves R factor allowing it to bond to gastric derived intrinsic factor

B12-IF complex absorbed in the terminal ileum

Normal B12 depends therefore upon:

Diet

Acid/pepsin in the stomach

Pancreatic protease

Intrinsic factor secretion by the stomach

Intact functioning ileum

Folate in contrast absorbed by small bowel throughout its length

Leafy veg, mushrooms, oatmeal, easily destroyed in cooking

MDR 200 - 400 μg per day

Causes of B12 Deficiency

Poor intake of meat:

vegetarians

elderly

alcoholic

anorexia, nervosa or aversive

Pernicious anaemia:

classic autoimmune disorder, present in 4%F and 2%M >60

Antibody to parietal cells in 70%

Antibody to intrinsic factor in 60 - 70%

Achlorhydria \leftarrow don't produce acid \leftarrow so unlikely to get reflux

Other gastric problem:

partial or total gastrectomy

bariatric surgery

Helicobacter pylori

PPI therapy

Absorptive problem:

small bowel disease especially Crohn's terminal ileum

Ileal resection

Blind loop syndrome

Coeliac disease

Pancreatic disease, exocrine failure

Sjogren's syndrome

HIV infection

Fish tapeworm

Causes of Folate Deficiency

Poor intake:

elderly

alcoholic

Poor absorption:

coeliac disease and other enteropathies

Increased requirements:

pregnancy and lactation

Haemolytic anaemias

Drugs:

trimethoprim, methotrexate, phenytoin

Effects of vitamin B12 Deficiency

Blood

pernicious anaemia
 macrocytosis (careful, may not be if Fe def as well)
 hypersegmented neutrophils
 pancytopenia *-refe*
 thrombocytopenia

Nervous system

peripheral neuropathy
 weakness
 paraesthesias
 ataxia
 tremor
 paraplegia

Subacute Combined Degeneration of the Cord

25% aren't anaemic
 non-stop tingling feet and hands
 degeneration of corticospinal tract
 paraplegia
 optic atrophy
 ✗ absent reflexes
 ✗ extensor plantars
 permanent if not treated

Gastrointestinal

glossitis
 stomatitis
 diarrhoea

Which patients should have a B12 estimation done??

- Tired
- Breathless
- Palpitations
- TATT
- Sore mouth and/or tongue
- also => iron estimat* Dysgeusia *-funny taste/metallic*
- Dizziness
- Pins and needles
- Unsteadiness
- Tremor
- Poor concentration
- Bad memory
- Irritability
- Depression
- Sleep disturbance

OR

Found to have:

- anaemia
- macrocytosis
- thrombocytopenia
- pancytopenia

Macrocytosis:

- alcohol
- drugs
- liver disease
- hypothyroidism
- folate def
- myeloma
- leukaemia
- myelodysplasia

Presentations can be varied and non-specific!!!

Interpretation of Results and Further Investigation

Normal range 150 – 900ng/l

likely to be signif.
x < 100 repeat and treat

Investigate cause:

Look again at history

Fe, B12, Fol

Parietal cell/ intrinsic factor antibody

Schilling test - *no longer available to do*

If multiple deficiencies suspect malabsorption

If diarrhoea or abd pain suspect Crohn's

Practice Point

Don't leave patient untreated with anaemia or possible neurology

100 - 140 Vegan : oral supplementation

100 - 150 meat eater, further investigation

How to Treat B12 Deficiency

only 10% gets absorbed
Im hydroxocobalamin 1mg daily or alternate days for 5 doses (loading)

Then 1mg weekly for one month

Then 1mg 3 monthly

as produces new cells so quickly
If anaemic check K and reticulocyte count on day 7 (should be > 7%)

Other preparations:

oral

Nasal spray

Patch

If folate defic must give B12 + folate to prevent subacute degeneration

What if patient doesn't get better?

Think of associated diseases:

adrenal insufficiency

Coeliac disease

Thyroid disease

PA increases risk of gastric Ca

Think chronic fatigue syndrome !!

Scenarios

24 yr old student feels tired all the time with poor concentration. FBC and profile normal but B12 level 136µg/l . Repeat.

58 yr old lady feels tired and breathless. Hb 98g/l with MCV 105fl. B12 =72µg/l
Pernicious anaemia . Start treatment.

32 yr old woman who had a right hemicolectomy for Crohn's disease 7 yrs ago feels tired. Hb117g/l but B12= 126µg/l . Long term replacement. *My.*

64 yr old lady with pins and needles in hands and feet, FBC normal but B12 = 110ug/l . Repeat . Treat . Refr neurologist .

48 yr old Asian lady feels exhausted all the time. Hb 110g/l, MCV 78fl, ferritin 98, B12= 143µg/l
*Thalassaemia . Prob not B12 defic .
? oral supplement -*

78 yr old man who had an op for a duodenal ulcer in his 20s loses weight and feels tired. Hb120g/l, MCV of 93fl, ferritin of 7µg/l and B12=138 µg/l
Partial gastrectomy . SCOPE ↓ could be gastric cancer

36 yr old alcoholic who you are asked to check over. His Hb is 110g/l with a ferritin of 1200µg/l, MCV 105fl, B12= 180ug/l, folate 3.4ug/l
think haemochromatosis if > 1000.

28 yr old woman you think looks pale. Hb 112g/l, ferritin 7ug/l, folate 1.5 ng/ml, B12 =135ug/l, Ca 1.97mmol/l
Celiac

42 yr old woman, absolutely exhausted, Hb 117g/l, B12= 142 ug/l. You treat with B12 but she feels no better. You note Na occasionally low at 129mmol/l

Addison's.