Guidance for Primary Care on the Interpretation of B12

* B12 deficiency does **not** usually require secondary care referral. Ask about OTC supplements prior to testing.
* **It is not appropriate to measure B12 in patients on IM treatment**. Monitor response to treatment using the full blood count (Hb and MCV).

**Clinical features of B12 deficiency**

*B12 levels are not easily correlated with clinical features, and low levels may not represent a functional B12 deficiency.*

Features of B12 deficiency may include:

* Macrocytic anaemia (MCV >101 fl)
* Glossitis
* Peripheral neuropathy (paraesthesia, unsteadiness, gait)
* Optic nerve dysfunction (blurred vison, atrophy, field loss)
* Unexplained fatigue

**Risk factors for B12 deficiency**

* **Medications**: metformin, PPI, H2 antagonists, anti-convulsants, colchicine
* **Vegetarian/vegan/poor or restricted diet without OTC supplements**
* **Existing GI disease/surgery**:atrophic gastritis, coeliac, bariatric surgery
* **Family history of B12 deficiency or auto-immune condition**
* **Pregnancy**: total B12 levels may be unreliable - use active B12.
* **Recreational nitrous oxide use:** total B12 levels are unreliable - use MMA.

**Likely B12 deficiency.**

Consider risk factors and underlying cause.

B12 197 – 771 ng/L

**Normal total B12 level.**

 If strong clinical suspicion of deficiency remains, **consider a trial of replacement** if total B12 is borderline normal.

MMA testing only if recommended by haematology/neurology or if nitrous oxide use.

If B12 is in upper half of reference range (>484ng/L),

B12 deficiency is unlikely. Investigate other causes + repeat in 3-6 months if still symptomatic.

B12 < 196 ng/L

**Consider Intrinsic factor antibodies (IFA)** if auto-immune gastritis is suspected.

IFA test will be added by laboratory if total B12 <150ng/L and if not performed previously.

B12 >771 ng/L

**Raised total B12 level**

High B12 in patients not on treatment may be due to consumption of OTC supplements or fortified food. It is rarely of clinical significance but can be associated with the following conditions:

* **Myeloproliferative disorders**

(unlikely if FBC normal)

* **Severe Liver disease**
* **Renal failure**

Guidance for Primary Care on the Interpretation of Folate

* **It is not appropriate to measure folate in patients on supplements.** Monitor response to therapy using the FBC (Hb and MCV).
* In the presence of true B12 deficiency, serum folate may be elevated.

Folate <3.0 μg/L

**Folate deficiency.**

Check B12 levels if not done in last year and commence folate replacement *(symptoms of B12 deficiency can be exacerbated if treated with folate replacement alone)*

Consider underlying cause.

**Causes of Folate deficiency**

* **Dietary deficiency/anorexia**
* **Pregnancy**
* **Alcoholism**
* **Malabsorption**

consider other features of malabsorption/pancreatic insufficiency.

* **Haemolysis**
* **Malignancy**
* **Medications:** Anti-convulsants
* **Sample collection immediately post-dialysis**

Folate 3.0 – 3.9 μg/L

**Possible folate deficiency.**

Exclude reduced intake over last few days.

Review symptoms/clinical features

**Severe**

**Mild/none**

**Review dietary intake and repeat in 6 – 8 weeks.**

**If still low, consider replacement.**

**Check B12 levels if not done in last year**

**Commence replacement.**

Folate >3.9 μg/L

**Folate deficiency unlikely.**

Serum folate reflects recent folate ingestion. Recent high dose biotin intake may cause falsely elevated results; please see <https://tinyurl.com/BiochemInfo> for more information on biotin interference.

If strong clinical suspicion of deficiency remains, rule out B12 deficiency and seek advice from haematology.

**Clinical features of Folate deficiency**

Features of folate deficiency include:

* Macrocytic anaemia (MCV >101 fl)\*
* Angular cheilosis/stomatitis

\*Note: co-existing iron deficiency/thalassaemia trait may mask macrocytosis

Guidance for Primary Care on the Interpretation of Ferritin

* For investigation of iron deficiency, serum ferritin is the recommended front line test and is superior to transferrin saturation.
* Monitor response to iron therapy using FBC (Hb and MCV) initially. **There is usually no need to re-check ferritin levels within 8-12 weeks.**

<15 μg/L

**Iron deficiency confirmed.**

Evaluate underlying cause and commence replacement.

15 – 30 μg/L

**Iron deficiency likely.**

Consider clinical context and commence replacement if appropriate.

Evaluate underlying cause

30 – 150 μg/L

**Iron deficiency unlikely.**

CRP <5 mg/L?

**Iron deficiency not excluded. Transferrin saturation will be added by laboratory.**

For patients with chronic inflammatory conditions, interpret ferritin cautiously.

Ferritin levels are increased independently of iron status in acute and chronic inflammatory conditions, malignancy and liver disease.

This may mask Iron deficiency.

Review FBC parameters and transferrin saturation (TSAT); if TSAT <16%, iron deficiency is possible.

*Note: transferrin saturation is non-specific as pregnancy, OCP and chronic illness can result in low transferrin saturation without iron deficiency.*

Yes

No

>150 μg/L

**Iron deficiency unlikely**

If Ferritin elevated above age and sex reference ranges and CRP normal

Refer to <https://tinyurl.com/BiochemInfo> for investigation of hyperferritinaemia.

**Causes of iron deficiency**

* **Inadequate diet or malabsorption**
* **Bleeding**, e.g. GI bleeding, menorrhagia or blood donation
* **Chronic renal failure** and haemodialysis
* **Infancy, pregnancy or lactation**
* **Increased red cell turnover.**

**Clinical features of iron deficiency**

Features of iron deficiency include:

* Microcytic hypochromic anaemia (MCV <79 fl)
* Symptoms of anaemia – fatigue, dyspnoea, pallor.
* Symptoms of iron deficiency may occur without anaemia: lack of concentration, irritability, hair loss, dry skin, angular cheilosis, atrophic glossitis, spoon-shaped nails, and unusual cravings for non-food items (phenomenon known as pica).