Guidance for Primary Care on the Interpretation of Haematinics

B12, Folate and Ferritin

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**Vitamin B12**

- B12 deficiency does **not** usually require secondary care referral.
- Replacement is usually given by IM injection. Oral replacement may be appropriate for mild deficiencies where the IFA result is negative.
- **It is not appropriate to measure B12 in patients on IM treatment.** Monitor response to treatment using the full blood count (Hb and MCV).

### Causes of B12 deficiency
- Pregnancy, OCP, HRT (not thought to represent a functional B12 deficiency)
- Medications: metformin, PPI, anti-convulsants e.g. phenytoin, antibiotics, colchicine
- Vegetarian/vegan/poor diet
- Malabsorption – consider other features of malabsorption/pancreatic insufficiency
- Pernicious anaemia – consider history of autoimmune disease and/or family history
- Folate deficiency
- Parasitic infection, HIV,

### 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
- Paraesthesia, unsteadiness, peripheral neuropathy

*Note co-existing iron deficiency/thalassaemia trait may mask macrocytosis
It is not appropriate to measure folate in patients on supplements. Monitor response to therapy using the full blood count (Hb and MCV).

Serum folate should always be measured with B12; in the presence of true B12 deficiency, serum folate may be elevated.

- **Folate <3.0 μg/L**
  - Folate deficiency.
  - Check B12 levels and commence folate replacement (symptoms of B12 deficiency can be exacerbated if treated with folate replacement alone)
  - Consider underlying cause

- **Folate 3.0 – 3.9 μg/L**
  - Possible folate deficiency.
  - ? Reduced intake over the previous few days
  - ? Symptoms/clinical features

- **Folate >3.9 μg/L**
  - Folate deficiency unlikely.
  - Serum folate reflects recent folate ingestion and recent high dose biotin intake may cause falsely elevated results; please see [https://tinyurl.com/BiochemInfo](https://tinyurl.com/BiochemInfo) for more information on biotin interference.

If strong clinical suspicion of deficiency remains, rule out B12 deficiency and consider discussion with haematology.

- **Check B12 levels**
  - Commence replacement.

- **Repeat in 6 – 8 weeks.**
  - If still low, consider replacement.

### 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

### 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
**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 no need to re-check ferritin levels within 6 – 8 weeks.**

<table>
<thead>
<tr>
<th>Ferritin Level</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>&lt;15 μg/L</td>
<td>Iron deficiency confirmed. Evaluate underlying cause and commence replacement.</td>
</tr>
<tr>
<td>15 – 30 μg/L</td>
<td>Iron deficiency likely. Consider clinical context and commence replacement if appropriate. Evaluate underlying cause</td>
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| 30 – 150 μg/L | CRP <5 mg/L? airy.  
  Yes: Iron deficiency unlikely.  
  No: Iron deficiency likely. |
| >150 μg/L     | Iron deficiency unlikely |

**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 which may mask deficiencies. Review FBC parameters and transferrin saturation; if <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.**

**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).