

## H.A015 – INVESTIGATION OF A RAISED FERRITIN RESULT

An elevated ferritin result (>200ug/L females, >300ug/L males) is a frequently occurring abnormality in clinical practice. This information sheet should be used as a guide for determining appropriate further investigations and management.

### What is ferritin?

Ferritin is a protein that is involved in the storage and release of iron. Under normal conditions the levels of ferritin reflect the amount of storage iron that is present in the body. Low levels are consistent with iron deficiency. Elevated levels are seen when body iron stores are increased. Ferritin levels will also mirror acute phase reactants (e.g. CRP) therefore clinical states which may result in inflammation such as infection, malignancy or inflammatory disorders will also cause an elevated ferritin.

### What are the causes of an elevated ferritin result?

Primary iron overload

- Hereditary Haemochromatosis/Genetic Haemochromatosis. (Approximately 90% of cases have a mutation in the causative HFE gene (C282Y homozygote, or C282Y/H63D compound heterozygote)

Secondary iron overload

- Metabolic syndrome (NIDDM, hypertension, obesity)
- Chronic haemolysis
- Excess iron supplements (usually parenteral)
- Prolonged Haemodialysis
- Chronic liver disease (alcoholic liver disease, porphyria cutanea tarda, Hepatitis B and C, non alcoholic steatohepatitis (NASH), Chronic porto-caval shunting)

'Reactive' causes

- Malignancy
- Inflammatory disorders e.g. rheumatoid arthritis, inflammatory bowel disease
- Acute and chronic infections
- HIV
- Acute alcoholism
- Acute or chronic hepatitis

Rare causes

- Non HFE related genetic haemochromatosis or hyperferritinaemia

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### **What further investigations are required if an elevated ferritin is discovered?**

A clinical assessment is advised in the first instance to consider reactive causes. If a reactive cause can be identified then this should guide further investigation e.g. suspected malignancy, evidence of infection, likely inflammatory disorder etc.

Where no reactive cause can be identified then it is recommended that the serum ferritin should be repeated with measurement of a fasting transferrin saturation.

Persons shown to have a persistently elevated ferritin and a fasting transferrin saturation >50% in males/>40% in females are at risk of having genetic haemochromatosis. In these individuals an HFE mutation screen should be requested (available on ICE requesting system; request "haemochromatosis mutations").

Persons who do not have an elevated transferrin saturation are very unlikely to have genetic haemochromatosis. Reactive causes and secondary causes should be reconsidered.

### **Which patients should be referred for further investigation?**

All patients who are found to have genetic haemochromatosis on HFE testing (i.e. are C282Y homozygous or C282Y/H63D compound heterozygote) should be referred for further management. Referral can be made to either the haematology department or the gastroenterology department. If the ferritin is >1000ug/L or if liver function tests (LFTs) are abnormal, then a Gastroenterology opinion in the first instance is indicated. When the patient attends the hospital they will be assessed for evidence of iron related end organ damage. For persons with confirmed iron overload a venesection programme to remove the excess iron will usually be offered.

For patients with a mild increase in ferritin and where other causes are not evident a period of observation is reasonable. For individuals who have a ferritin >1000ug/L or deranged LFTs or where there is suspicion of an underlying medical disorder a referral to gastroenterology is advised.

### **Consultation process**

This advice leaflet was written by the Department of Haematology and consultation with the Gastroenterology Department at the Norfolk and Norwich University Hospital.

### **Reference**

Cullis JO et al. Investigation and management of a raised serum ferritin (2018) British Journal of Haematology 18(3): 331-340

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