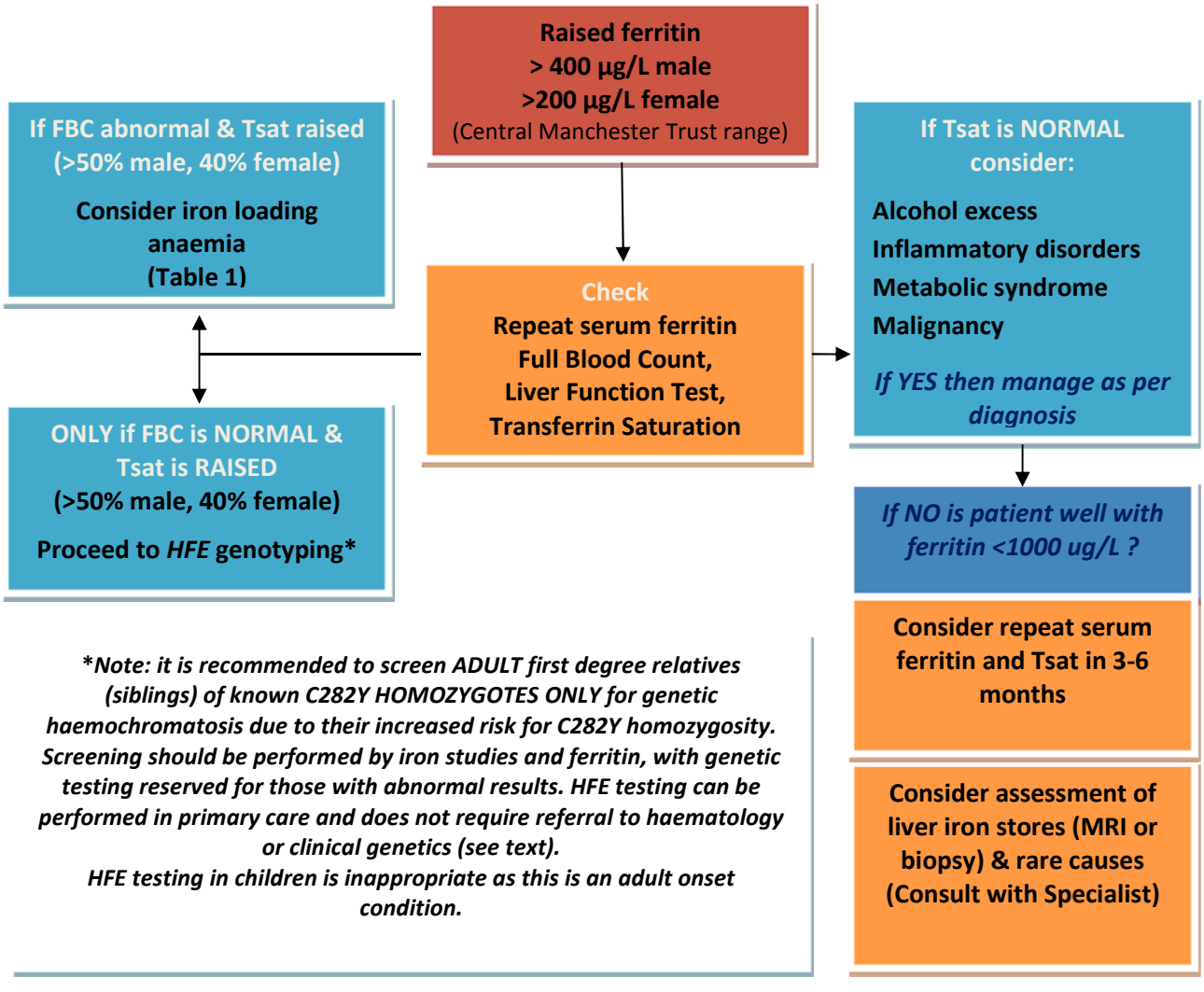
Hyperferritinaemia

High Serum Ferritin results are a common finding in primary care. Because ferritin is an acute phase reactant this is usually due to inflammation, malignancy or liver disease. It can less commonly be associated with iron overload. This guide is designed to aid primary care physicians investigating hyperferritinaemia, the main causes of which are listed in **Table 1** overleaf.

The ferritin range in the Central Manchester University Hospital laboratory are 30 - 400 µg/l for a male and 13 - 150 µg/l for a female. However Serum Ferritin levels can vary with age.

Hyperferritinaemia should not automatically generate a *HFE* gene mutation test or a referral to a Consultant Haematologist and general investigation should proceed as per the algorithm below. The patient should be questioned about alcohol intake and other risk factors for liver disease, transfusion history, family history of iron overload, and signs/symptoms of malignancy and inflammatory disorders.

Algorithm for investigating hyperferritinaemia in patients without known secondary iron overload



Considerations when investigating hyperferritinaemia

- Transferrin saturations do not need to be performed on fasting samples but this may be required if there is a borderline reading.
- In addition to the above algorithm and table 1 below, if investigating other causes, consider a viral hepatitis screen and abdominal ultrasound if liver function abnormal and blood glucose and lipid studies.
- If both Serum Ferritin and Transferrin Saturation are raised then *HFE* genotyping is indicated.
- HFE screening can be requested and performed in primary care and does not require a referral to the clinical genetics team, 7mls of blood in a EDTA is required and is sent to the local hospital laboratory who will then forward on. Please note that the mutations screened for are those common to the Caucasian population and are unlikely to be relevant to other ethnic groups, however the prevalence of haemachromatosis in the non-Caucasian population is very low.
- If the patient is found to be homozygous for the C282Y mutation or compound heterozygous for C282Y/H63D then referral (to the patient's local hospital) for venesections is indicated. . This should be in conjunction with managing other contributing risk factors such as alcohol consumption, fatty liver disease and metabolic syndrome). Carrier status for the HFE gene is 1 in 9 in the population and is not normally associated with health problems.
- If the Transferrin Saturations are normal and the Serum Ferritin is >1000µg/L, referral to a Hepatologist is required.
- If TS and ferritin high and *HFE* genotyping is negative or shows heterozygous states for the common haemachromatosis mutations, referral to a Hepatologist is advised for in depth quantification of liver iron. In patients with a severe iron overload phenotype, other rare forms of hereditary haemochromatosis cannot be excluded.

Increased Ferritin synthesis due to iron accumulation	**Increase in Ferritin synthesis not associated with significant iron accumulation**	**Increased Ferritin as a result of cellular damage**
Secondary iron overload from blood transfusion or excessive iron intake/administration Hereditary (Genetic) Haemochromatosis Hereditary aceruloplasminaemia Ineffective erythropoiesis: sideroblastic anaemia, some myelodysplasias (e.g. refractory anaemia with ring sideroblasts) Thalassaemias Atransferrinaemia FPN1 haemochromatosis	Malignancies Malignant or reactive histiocytosis Hereditary hyperferritinaemia with and without cataracts Gaucher's disease Acute and chronic infections Chronic inflammatory disorders Autoimmune disorders	Liver diseases including: Liver necrosis, Chronic viral hepatitis, Alcoholic and non-alcoholic steatohepatitis* Chronic alcohol consumption * May also have iron overloading