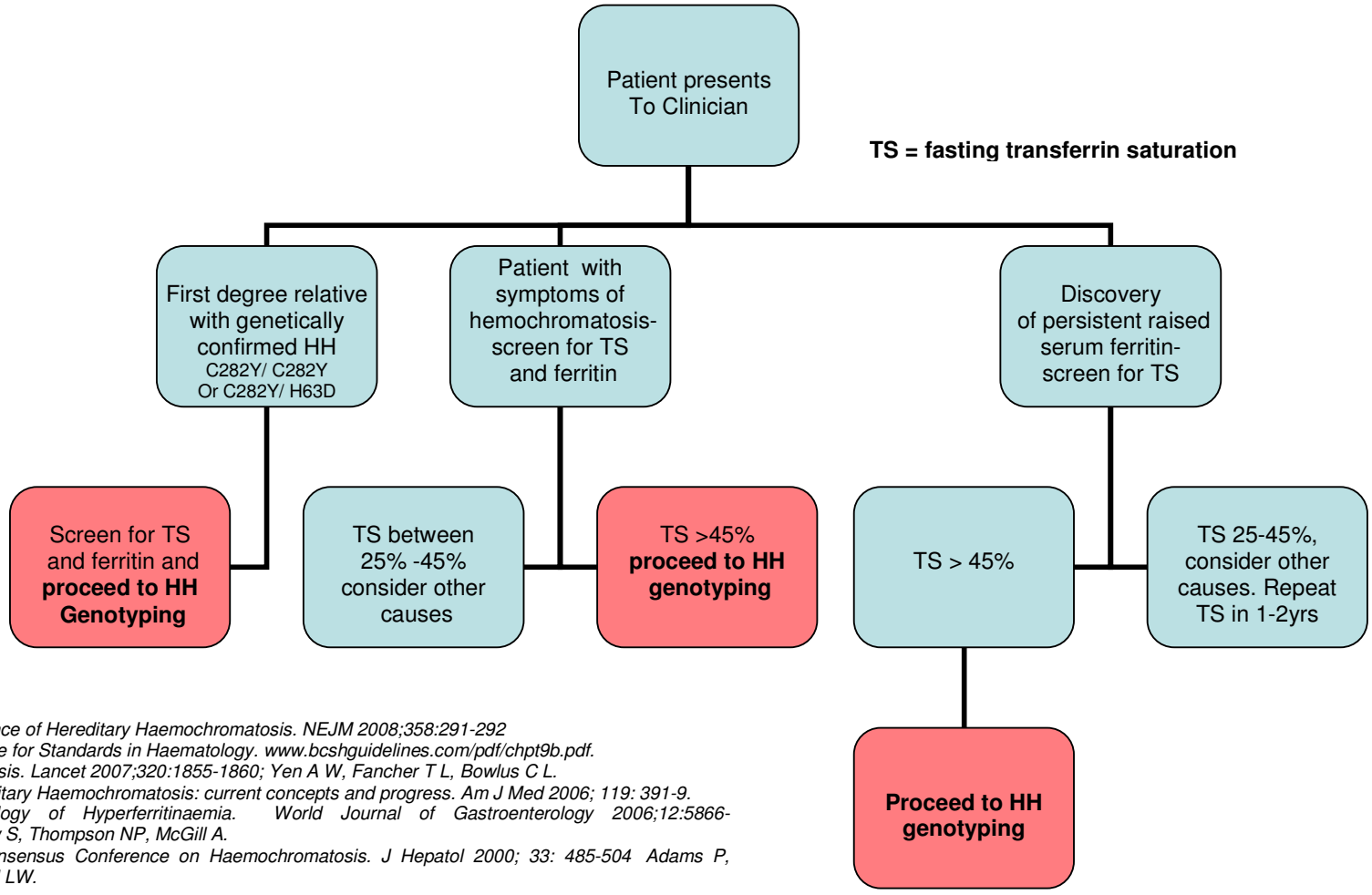
INVESTIGATION PROTOCOL / GUIDELINE FOR HAEMOCHROMATOSIS



REFERENCES

Clinical Penetrance of Hereditary Haemochromatosis. NEJM 2008;358:291-292

British Committee for Standards in Haematology. www.bcshguidelines.com/pdf/chpt9b.pdf.

Haemochromatosis. Lancet 2007;320:1855-1860; Yen A W, Fancher T L, Bowlus C L.

Revisiting Hereditary Haemochromatosis: current concepts and progress. Am J Med 2006; 119: 391-9.

**The Epidemiology of Hyperferritinaemia. World Journal of Gastroenterology 2006;12:5866-5869.Hearnshaw S, Thompson NP, McGill A.*

International Consensus Conference on Haemochromatosis. J Hepatol 2000; 33: 485-504 Adams P, Brissot P, Powell LW.

INTERPRETATION OF HFE GENOTYPING RESULTS

C282Y/C282Y (C282Y Homozygote)

Approximately 90% of Irish patients with hereditary haemochromatosis (HH) are homozygous for the C282Y mutation. Gene penetrance is variable and a proportion of individuals with this genotype do not develop clinical haemochromatosis

C282Y/H63D (Compound Heterozygote)

Approximately, 5% of patients with HH have this genotype. Some patients with this genotype have iron overload but to a lesser degree than C282Y homozygotes.

C282Y/Normal (C282Y Heterozygote)

A small proportion of C282Y heterozygotes exhibit mild to moderately raised indices of iron-overload. Complications due to iron-overload are rare and may be influenced by additional factors, both genetic and environmental.

H63D/H63D (H63D Homozygote)

This genotype is present in about 2% of the population and its role in the development of haemochromatosis remains unclear. The risk of iron-overload in these patients is low.

Procedure for genetic sampling

Discuss with patient and obtain informed consent and complete the HH request form.

Consider referral

C282Y homozygote (C282Y/C282Y) with raised ferritin, compound heterozygotes (C282/H63D) with raised ferritin +/- abnormal LFTs.

Patients with liver or endocrine abnormalities should be sent to these sub specialities.

Note: Ferritin <1000 ng/ml is rarely associated with tissue damage. If ferritin persistantly >1000 ng/ml,

Pitfalls in diagnosis

*Ferritin is a liver synthesised acute phase reactant. Factors causing raised ferritin not related to iron overload include; liver disease, alcohol, chronic inflammation/infection, neoplasia, renal disease, and chronic haemolytic anaemia/ thalassemia. Medical investigations of secondary causes of elevated ferritin should be led by patients' symptoms and signs.

It is possible that mutations or polymorphisms in modifier genes are involved in determining a severe disease phenotype in HH. Some rare cases of iron-overload are not linked to mutations in the HFE gene. They are associated with other forms of 'genetic haemochromatosis' and linked to mutations in different genes requiring specialist testing.

Some groups may have normal transferrin saturation (TS) but have genetic haemochromatosis. These include: blood donors, women with menorrhagia, children, young women and patients with chronic blood loss/bleeding disorders.

Results, which do not fall into a clear pattern, should be discussed with a Gastroenterologist, Haematologist or Endocrinologist.

Treatment goals

Phlebotomy: All patients with HH and ferritin >400ug/l and rising: venesection once weekly (450-500mls) until serum ferritin is <50ug/l and transferrin saturation is <50%.
Maintenance requires regular venesection 2-8 time yearly to maintain TS<50% and Ferritin<50 µg/L