Haemochromatosis

Introduction

- Hereditary haemochromatosis (HH) now easily screened for as most symptomatic individuals are homozygous for the C282Y mutation in the HFE gene
- 1 in 200 of Caucasian populations are homozygous
- There is variable expression ranging from asymptomatic (often just a raised transferrin saturation) to those with ‘bronze diabetes’; many will have subtle symptoms and modest elevation of ferritin
- Penetrance depends on age, iron losses (blood donation or menstruation lessen burden) and alcohol use

What to look for?

- Symptoms are non-specific and include: fatigue, arthralgia, loss of libido, abdominal pain
- Typical signs: hepatomegaly, diabetes, pigmentation, arthropathy (hips, knees and particularly 2nd and 3rd metacarpophalangeal joints)
- Check iron indices in anyone with raised ALT and in those with combination of above symptoms / signs

Investigating suspected haemochromatosis

- If raised ferritin and transferrin saturation, send 5mls EDTA blood sample for HFE genotyping to Molecular Genetics Laboratory, Box 143 Addenbrookes Hospital
- If homozygous then family screening as below

When to refer to hepatology?

- HH with ferritin > 1000mg/L or raised ALT, or non-HH iron overload: refer to Hepatology as may need liver biopsy
- HH with ferritin < 1000 and normal ALT: no biopsy as minimal risk of liver fibrosis but venesect if ferritin > 400 (refer Hepatology or local venesection service if available, aiming for ferritin of 50)
- NB non-HH genotype + mildly raised ferritin / ALT = likely fatty liver

Family screening for relatives of C282Y homozygotes or C282Y/H63D with abnormal iron studies

- Siblings should have HFE / iron indices checked
- Children tested only when adult but can screen partner/spouse to see if carrier (children only at risk if spouse is carrier = 10% chance)
- Parents if symptoms suggestive of HH (The risk is low otherwise)
- HH genotype + ferritin <200: reassure and monitor 2-5 yearly (less frequent if female, compound heterozygote, or no evidence of iron accumulation)
- HH genotype + ferritin 200-400: reassure and suggest blood donation via NBS up to 4 x year to prevent further iron overload (check iron indices annually)
- HH genotype + ferritin >400 see ‘When to refer to hepatology?’ points 1 and 2
- Refer to Medical Genetics Dept Box 134, Addenbrooke’s Hospital if: 1) index case genetics unknown 2) uncertain re counselling 3) index case not homozygous but family request (these cases may be advised by Genetics Clinic appointment or letter only)

Support group: British Haemochromatosis Society

Reference: Bradley-Smith, G., Hope, S., Firth, H.V., Hurst, J.A. 2010. Oxford Handbook of Genetics. Oxford University Press