NB Medical education

KISS: Hereditary Haemochromatosis

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⇨ **Cause**

- An inherited genetic disorder, autosomal recessive, which is associated with a defect in hepcidin, an iron regulating hormone, resulting in increased intestinal absorption of iron and subsequent deposition in the liver, pancreas, heart, skin, joints and gonads leading to organ damage
- *Prevalence is 1 in 200-250 in Northern European populations,* the most commonly affected group.
- Up to 85% is due to a mutation in the human haemochromatosis protein (HFE) gene being expressed through C282Y homozygosity, though other genes are also implicated. Penetrance of the genes, that is those who are subsequently affected as a result, is not 100%

⇨ **Presentation**

- Around 30% of patients may be asymptomatic throughout life, especially women where blood loss through menstruation and child birth is somewhat protective.
- When present, ***symptoms may be non-specific:***
  - Lethargy, arthralgia, vague abdominal complaints
  - **Abnormal LFTs**
    - This is the most common avenue to diagnosis in primary care
  - Arthropathy, chondrocalcinosis, heart failure, erectile dysfunction, porphyria cutanea tarda
  - "Classical presentation" due to end organ damage only seen in 10% of cases
    - Liver cirrhosis, diabetes, skin pigmentation (a bronze tan in the UK winter is a warning sign)

⇨ **Diagnosis**

- **Be suspicious for haemochromatosis**
- **Ferritin levels are raised and transferrin saturation is >45%**
  - Check serum ferritin
  - If ferritin raised check transferrin saturation
  - Exclude other causes of raised ferritin e.g. infection, inflammation, alcohol, etc.
- **If ferritin raised and transferrin saturation >45% refer to gastroenterology for genetic testing**, phlebotomy and assessment of end organ damage

⇨ **Treatment**

- The mainstay of treatment is bloodletting. This is secondary care led.
  - Maintenance aims to keep ferritin between 50-100ug/L
  - If no cirrhosis is present, patients should have a normal life expectancy
  - There is increased risk of osteoporosis so a DEXA scan should be performed.
- A ferritin of >1000ug/L at presentation is associated with a 20-45% risk of developing cirrhosis. These patients will be considered for liver biopsy as cirrhosis confers a 3-4% annual risk of hepatocellular carcinoma. Patients with cirrhosis should be enrolled in a HCC and oesophageal varices surveillance program.

⇨ **Should the family have genetic testing?**

- Siblings should be screened (they'll have a 25% risk of having the condition) with serum ferritin and transferrin saturation
  - Ideally they would have HFE genotyping with genetic counselling
- Partner testing can guide whether children require testing.