# Iron Overload in an H63D Homozygote: Looking Beyond the Genotype

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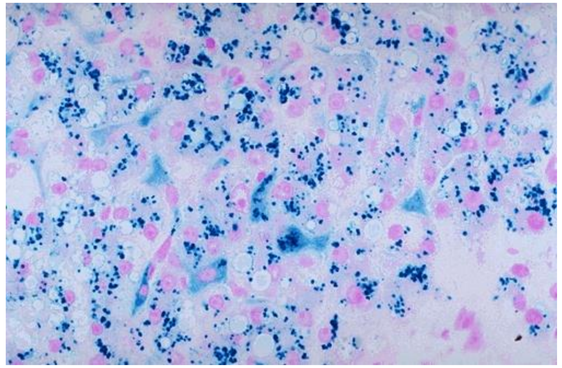
## Introduction

- Genetic disorder
- Excessive gastrointestinal absorption of iron
- Damage to liver and other organs
- Inheritance: autosomal recessive
- Mutations in the *HFE* gene
- Low penetrance
- Most common pathologic mutations: C282Y and H63D.
- Homozygous  C282Y – over 90% cases
- Remaining: C282Y/H63D compound heterozygosity, H63D homozygosity, or S65C mutation.
- A rare case of newly diagnosed HH in a patient with H63D homozygosity and family history of iron overload.

## Case

- 67 yo Caucasian male
- Chief complain: abnormal iron studies
- Past medical history: hyperlipidemia
- Family history: father needing phlebotomy.
- Social history: 2 alcoholic beverages daily



https://webpath.med.utah.edu/LIVEHTML/LIVER018.html#:~:text=A%20Prussian%20blue%20iron%20stain,disease%2C%20or%20numerous%20transfusions).

## Work up

- serum ferritin: 1240 ng/mL
- transferrin saturation: 45.6%
- Hemoglobin: 15.5 g/dL
- ALT: 91 units/L
- AST: 43 units/L
- Genetic testing: homozygosity for H63D
- liver biopsy: diffusely increased iron deposition mostly in hepatocytes.
- Moderate steatosis and portal fibrosis (fibrosis stage 1/4)
- Diagnosis of HH made
- Phlebotomy - goal ferritin <50 ng/mL

## Discussion

- Majority - C282Y homozygosity
- Clinically significant iron overload - less common with homozygous H63D: < 10% of all HH cases.
- Higher likelihood of iron overload if 1st degree relative has iron overload
- Higher risk of liver disease in our patient: HH and hepatic steatosis
- To reduce risk:
  - control of ferritin via phlebotomy
  - modification of other risk factors (weight, hyperlipidemia)
- importance of evaluating for HH and hepatic fibrosis in patients with phenotypic signs of iron overload and family history - irrespective of genotype.