Inside Out: Gastroenterology & Hepatology Workshop

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Clinical Skills Development Service | RBWH

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Metro North Health

High Ferritin

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Metro North Hospital and Health Service

High Ferritin

Gastroenterology/Hepatology GP Education Event
25 October 2025

Prepared by: Dr Anthony Deacon, Gastroenterologist & Hepatologist (Redcliffe, RBWH, STARS)

Metro North Health | Queensland Government

Overview

Presentation Outline

1. Iron Physiology
2. Interpretation of Iron Studies
3. Causes of Elevated Serum Ferritin
4. Ferritin and Alcohol
5. Assessment of Elevated Ferritin
6. When to Refer
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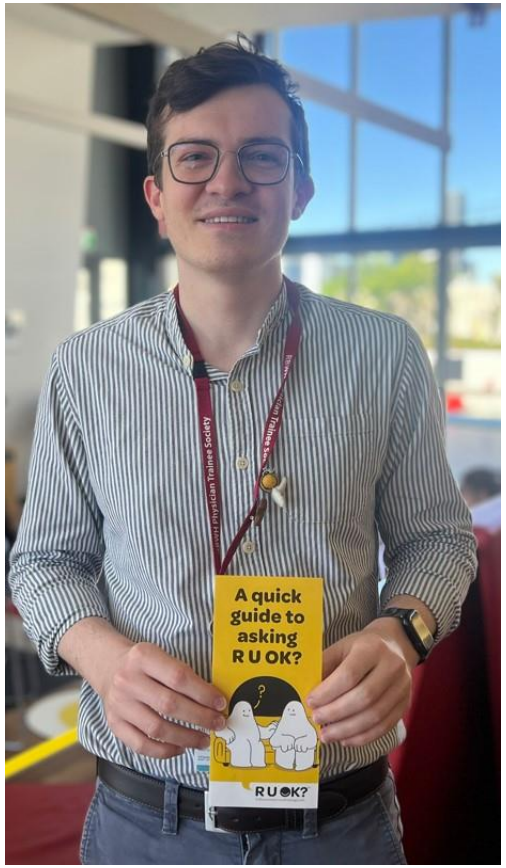
8. Hereditary Haemochromatosis (HH)
9. HFE Gene
10. Non-HFE HH
11. Management of HH
12. High Ferritin App
13. Causes of Secondary Iron Overload
14. Case Studies 2, 3 and 4

About the Presenter

- **Dr Anthony Deacon** is a consultant gastroenterologist currently practicing at Redcliffe Hospital, the RBWH and STARS.
- He completed his Fellowship in Gastroenterology and Hepatology in 2023, following a dedicated fellowship year in inflammatory bowel disease, intestinal failure, and home parenteral nutrition.
- His clinical interests include hepatology, IBD, general endoscopy and parenteral nutrition.
- Anthony also serves as the President Elect of the Adult Medicine Division of the RACP, the Secretary of the Gastroenterological Society of Queensland (GESQ), and a committee member of the RACMA QLD/NT Jurisdictional Committee.
- Please feel free to contact him with any questions at anthony.deacon@health.qld.gov.au



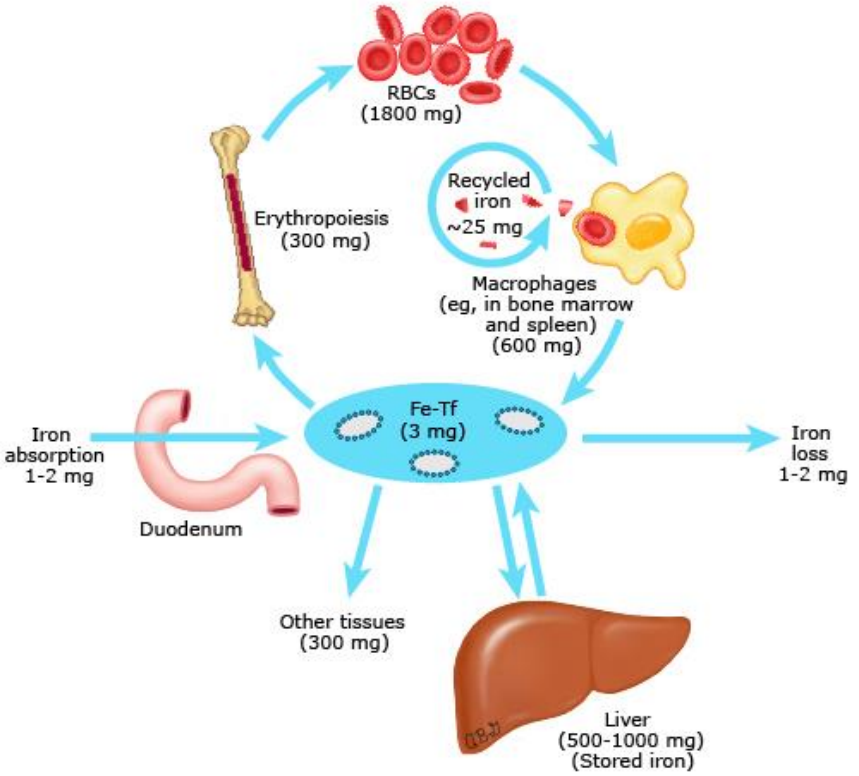
Overview

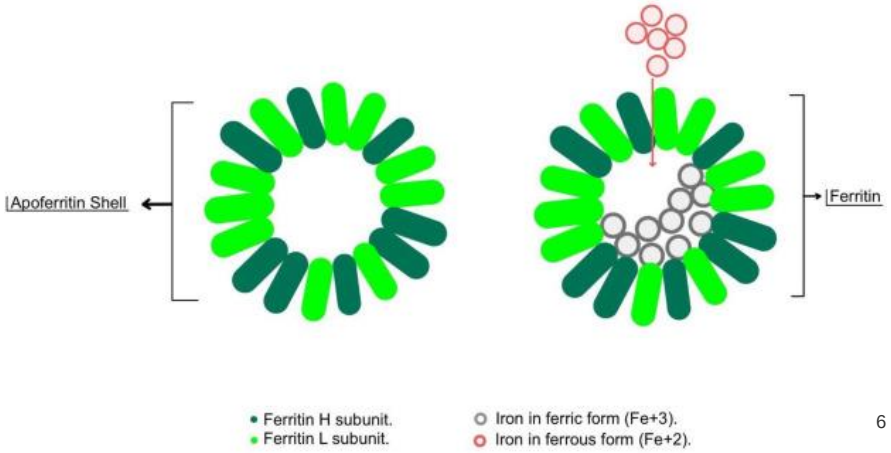
*Medicine is an **art not a science**. When managing a patient with an elevated ferritin, it is almost never an emergency* because of the length of time it takes for iron to accumulate, so **you have the benefit of time to reassess (the science) to formulate an impression (the artwork).***

** Exceptions include iron poisoning/overdose and a serum Ferritin in the many 1000s*

Iron Physiology

- **Body Iron Distribution:** Total body iron is ~3–4 grams; ~75% is in haemoglobin, ~10–20% is stored as ferritin, and the rest is in myoglobin, enzymes, or bound to transferrin.
- **Iron Absorption & Loss:** Only ~1–2 mg of iron is absorbed daily (≈10% of dietary intake) to balance ~1–2 mg daily losses (sloughed cells) . Absorption occurs in the duodenum and is tightly regulated by the liver-produced hormone **hepcidin**, which decreases iron absorption and release.
- **No Active Excretion:** The body lacks an active iron excretion mechanism. Iron homeostasis relies on regulating absorption via hepcidin. Excess iron is stored in ferritin within tissues (liver, spleen, bone marrow) to prevent toxic free iron.
- **Transferrin & Ferritin:** Transferrin is the transport protein that carries iron in blood; transferrin saturation (TS) indicates how much iron is bound. Ferritin is a storage protein that sequesters iron; serum ferritin correlates with total iron stores but is also an acute phase reactant.
- **Iron Toxicity:** Free iron catalyzes formation of reactive oxygen species, so it must be bound to proteins. In iron overload, excess iron deposits as ferritin and haemosiderin in organs, causing oxidative damage, inflammation, and fibrosis in tissues (especially liver, heart, pancreas, joints, endocrine organs).





Interpretation of Iron Studies

- **Key Laboratory Measures:**
  - **Serum Iron:** Iron circulating in blood (used alone only in specific circumstances → **ignore**)
  - **Total Iron-Binding Capacity (TIBC):** Indirect measure of transferrin levels (used alone only in specific circumstances → **ignore**)
  - **Transferrin Saturation (TS):** Serum Iron ÷ TIBC × 100. This is **critical** for assessing iron status.
    - **TS > 45%** is suggestive of iron excess (iron overload), and >55% increases specificity for hereditary hemochromatosis (HH).
    - **A TS < 45%** makes significant iron overload unlikely.
    - TS is often the earliest indicator of iron overload in HH, sometimes becoming elevated even before ferritin rises.
  - **Serum Ferritin:** Reflects stored iron. Low ferritin is a sensitive indicator of iron deficiency. High ferritin indicates increased iron stores but is **non-specific.**
    - There is no recommended harmonised upper reference interval value for ferritin as significant variation exists between methods. Expected values for the upper reference interval quoted by manufacturers of some commonly used assays range from 275 to 400ug/L (male adults) and 150 to 307 ug/L (female adults).
    - The Serum Ferritin is the best test to screen for iron overload. Levels over >1000 should raise concern for primary iron overload.
- **Transferrin Saturation Emphasis:** A **high ferritin with normal TS usually points to secondary causes** (inflammation, MASLD, alcohol, etc.) rather than true iron overload. Conversely, a consistently elevated TS suggests body iron loading and warrants further evaluation for hemochromatosis or other iron overload conditions.
- **Iron Overload vs Non-Overload: True iron overload** is typically defined by **elevated ferritin and transferrin saturation >45% (or >50%)**

Interpretation of Iron Studies

Haematinics

Test Name	Result	Reference Interval	Units
Iron	27	5 - 30	umol/L
Transferrin	2.2	1.9 - 3.1	g/L
TIBC	56	47 - 77	umol/L
Saturation	48 H	20 - 45	%
Ferritin	113	30 - 300	ug/L

Comments

High transferrin saturation in the presence of normal ferritin raises the possibility of early or treated haemochromatosis or recent iron ingestion.

Group discussion: what would you do next?

Causes of Elevated Serum Ferritin

- **Elevated ferritin is common in primary care**. Up to 20% of men have elevated ferritin; in women the prevalence ranges from about 3% in premenopausal to 17% in those older than 70. Fewer than 10% of hyperferritinaemia cases are due to iron overload Zhang, 2025, MJA; Goot, 2012 AFP).
- **Primary Causes of true iron overload (total body or hepatic):**
  - Hereditary haemochromatosis both HFE and Non-HFE (very very very rare)
- **Secondary Causes of true iron overload (total body or hepatic):**
  - Transfusional iron overload, including MDS with transfusions
  - Haemolytic and Iron-loading anaemias (thalassaemia major, sideroblastic anaemia)
  - Excess parenteral or oral iron
  - Porphyria cutanea tarda

TRANSFERRIN SATURATION ***HIGH***

- **No iron overload (secondary hyperferritinaemia):**
  - Alcohol-related liver disease
  - Metabolic associated steatotic liver disease and metabolic syndrome
  - Chronic viral hepatitis B or C
  - Acute or chronic inflammation and infection
  - Malignancy
  - Thyrotoxicosis
  - Chronic kidney disease
  - ***Adult-onset Still disease and haemophagocytic syndromes – special case***

USUALLY, TRANSFERRIN SATURATION ***NORMAL***

Ferritin and Alcohol

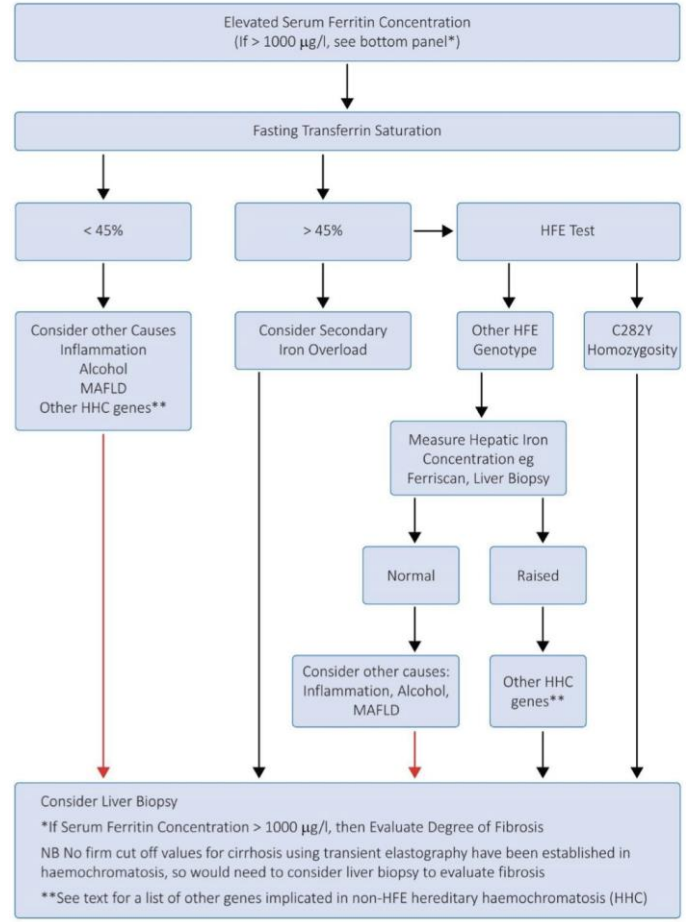
- **Alcohol's Effect on Ferritin:**
  - Chronic alcohol use increases iron absorption from the gut **and** ferritin synthesis **and** ferritin release from the liver.
  - Acute hepatic inflammation from alcohol or other causes (such as in alcoholic hepatitis) causes ferritin release from the liver.
- **Laboratory Clues to Alcohol Use:**
  - An elevated GGT is a sensitive marker of chronic alcohol intake, often accompanying high ferritin.
  - Other hints include an AST:ALT ratio > 2 and an elevated MCV (macrocytosis) in heavy drinkers.
  - If a patient with high ferritin has these findings (high GGT, AST>ALT, macrocytosis), consider alcohol as the most likely contributing factor.
- **Reversible with Abstinence:**
  - Ferritin elevations from alcohol are reversible.
  - It's often recommended to have the patient abstain from alcohol for 6-8 weeks and then repeat ferritin - a significant drop supports alcohol as the cause of high ferritin.
- **But do heavy drinkers develop anaemia in the absence of other causes?**
  - In advanced alcohol related liver disease, there is often slow gastrointestinal bleeding (e.g. from PHG, GAVE, Angioectasias), decreased erythropoietin production, and decreased transferrin production.
  - Together this leads to a loss of RBCs and decreased RBC production.
  - Alcohol also directly supresses bone marrow, often accompanies by leukopenia and thrombocytopaenia (the latter can be from portal hypertension also)

Assessment of Elevated Serum Ferritin

1. **Assess for Common Causes:** A raised **serum ferritin** is often multifactorial. Assess for:
   - **Anaemia** with an FBC
   - **Liver Function Abnormalities**, with LFTs **and Hepatitis B and C serologies and an ultrasound if elevated**
   - **Inflammation** if inflammatory markers are raised
   - **Metabolic comorbidies** (Obesity, HTN, Dyslipidaemia, DM), **especially MASLD**
   - **Excess alcohol use**
   - *Also consider checking **thyroid function** (hyperthyroidism can raise ferritin)*
2. **Confirm Iron Studies:** Repeat fasting iron studies alongside inflammatory markers

If Serum Ferritin <1000, TS <45% and a secondary cause identified → monitor and manage as indicated

3. **Perform a HFE Genotype if TS > 45% and/or Ferritin >1000**
   - If HH is suspected (TS >45%, Elevated Ferritin and C282Y/C282Y genotype), consider referral to Lifeblood and refer to hepatology (please refer if Ferritin has ever been >1000 in this setting)
   - If the cause remains uncertain, manage comorbidities as above and refer to hepatology
5. **Avoid Premature Venesection:** Do **not initiate therapeutic venesection** before confirming true iron overload. Most cases of elevated ferritin (≈90%) are not due to haemochromatosis.



GESA Guideline

When to Refer and to Who

- **Indications for Specialist Referral:**
  - **Ferritin >3000 µg/L:** particularly if this is acute likely represents significant pathology (e.g. severe hepatitis, Still's disease, HLH) and warrants discussion with the GE Registrar on call (please perform LFTs)
  - **Ferritin >1000 µg/L** or **evidence of organ damage**:
  - **Hereditary Haemochromatosis confirmed (HFE: C282Y/C282Y) or strongly suspected**
  - **Unclear Cause or Complex Cases:** If the cause of elevated ferritin remains unclear after initial workup and it is persistent, or if there are coexistent issues (e.g. abnormal LFTs without obvious diagnosis, suspicion of non-HFE haemochromatosis, etc.).
- **Refer to the Right Specialty:**
  - Most patients with iron overload or unexplained high ferritin are managed by **Gastroenterology/Hepatology**
  - **Consider Haematology referral** if the context suggests a haematological issue: for example, a patient with **ferritin elevation plus cytopenias or haemolysis**
  - If in doubt about the cause, a referral to either service for initial evaluation is appropriate, and they will redirect as needed.
- **Referral Urgency and Advice:**
  - While elevated ferritin is **almost never an emergency** (iron accumulates over years, allowing time for workup), exceptions exist
  - For routine cases, take time to complete the workup and manage comorbidities before referral

When to Refer and to Who

Minimum Referral Criteria

Category 1 (appointment within 30 calendar days)	• Evidence of iron overload with liver decompensation (e.g. jaundice and/or ascites and/or encephalopathy)
Category 2 (appointment within 90 calendar days)	• Elevated serum ferritin level **without** presence of concerning features
Category 3 (appointment within 365 calendar days)	• Normal ferritin with positive HFE gene study (e.g. C282Y homozygosity or compound heterozygosity (C292Y/H63D))

2. Essential referral information Referral will be returned without this

- General referral information including details of presenting issues
- Comorbidities and past medical history
- Alcohol history
- Height, weight and BMI
- FIB-4 (Fib-4 calculator), ELFT, FBC results less than 3 months old
- HBV, HCV serology, fasting glucose and lipid results
- Iron studies
- HFE gene studies
- Recent upper abdominal ultrasound or CT reports

3. Additional referral information Useful for processing the referral

- Family history of liver disease or blood disorders
- Medication history including complementary and alternative medicines Previous liver function tests
- CRP

Case Study 1

- **Background:** A 52-year-old male with obesity and type 2 diabetes is noted to have persistently elevated liver enzymes on a routine check. Physical examination shows an elevated BMI and hypertension, There are no stigmata of chronic liver disease. The patient has had no preventative health actions taken as he has only seen you twice.
- **Initial Pathology Results:**
  - **Ferritin:** 920 µg/L (Ref range ~30–300) – markedly high.
  - **Transferrin Saturation:** 42% (Normal ~20–45%) – borderline high normal.
  - **FBC:** normal, platelets 140
  - **Bilirubin & Albumin:** normal
  - **ALT:** 50 U/L (Normal < 45); **AST:** 65 U/L (Normal < 40). AST:ALT ratio ~1.3
  - **GGT:** 400 U/L (Normal < 60). **ALP**: 90 (Normal <110)
  - **CRP:** 15 mg/L (Normal < 5).
  - **HFE Genetic Test:** C282Y/H63D **compound heterozygote** (one copy of each mutation).
- **Fibrosis Assessment:** To evaluate liver fibrosis risk, a **FIB-4 score** is calculated as 3.4 – which falls in the “high” range.

Case Study 1

- **MCQ1:** Given the patient's profile, **what is the most likely explanation for his initial high ferritin?**
  a) Hereditary haemochromatosis due to HFE compound heterozygous mutations
  b) Iron overload from metabolic syndrome
  c) Secondary hyperferritinaemia from multiple causes
  d) Acute phase reaction due to a chronic inflammatory state

- **MCQ2: What is the BEST initial management step for this patient's elevated ferritin?**
  a) Immediate therapeutic venesection in general practice, targeting ferritin <50 µg/L
  b) Repeat iron studies in 6 months
  c) Addressing reversible causes (alcohol cessation, weight loss for MASLD) and repeat assessment
  d) Addressing reversible causes (alcohol cessation, weight loss for MASLD) and referral to hepatology

Case Study 1

- **GP Action:** Suspecting mixed causes for hyperferritinaemia, the GP initiates lifestyle interventions (improved diet, weight loss, and alcohol cessation support). However, concerned about the ferritin of 920, the GP also decides to perform **therapeutic venesections** in primary care. Two 500 mL venesections are done one month apart.
  - **Follow-up Iron Studies (after 2 venesections):**
    - Ferritin is now **30 µg/L** (subnormal, ref >30), and transferrin saturation is **10%** (low).
    - **Haemoglobin** dropped from 150 g/L to 125 g/L (Normal 130–170) with **MCV 80 fL** (borderline), indicating onset of **iron deficiency with anaemia**.
  - The patient's fatigue has worsened, and he is asking if he should continue venesections.

- **Group Discussion:** Now that the patient has become **iron deficient after venesection**, **what should be done next?**
  - Consider how to manage his iron studies?
  - Does this patient need referral and why?
  - What history would you take? What other tests would you request?

Hereditary Haemochromatosis

- **Definition:** Hereditary haemochromatosis is an **autosomal recessive** genetic disorder causing inappropriate iron absorption from the gut, leading to **progressive iron overload**.
  - Excess iron is deposited in tissues, causing organ damage.
  - The **HFE gene** on chromosome 6 is most commonly implicated. **C282Y** is the principal mutation (cysteine-to-tyrosine at position 282)
- **Epidemiology:**
  - Approximately **1 in 200 Australians** are C282Y homozygous (prevalence ~0.5%).
  - Despite this, clinical penetrance is low - not everyone with the genotype develops iron overload. The male:female ratio for iron overload is about 5:1.
  - A 2008 Victorian study shows proportion of C282Y homozygotes with documented iron-overload–related disease was 28.4% for men and 1.2 for women The male:female ratio for clinical disease is about 5:1, due primarily to physiological blood and iron loss in women secondary to menstruation and pregnancy.
- **Clinical Features:** Classic HH often presents in mid-life (30s–50s in men, post-menopausal in women) with fatigue, arthralgias (especially hand joints), and nonspecific symptoms. Now it it is usually picked up prior to disease manifestations.
  - If untreated, organ damage can occur: cirrhosis, HCC, pancreatic atrophy, diabetes mellitus, hyperpigmentation, arthropathy, cardiomyopathy, hypogonadism.
- **Natural History:** Iron accumulation in HH is gradual. It typically takes years of excess absorption for significant organ damage to occur. Early diagnosis (before cirrhosis or diabetes) yields an excellent prognosis if treated. Once ferritin is controlled and iron removed, many symptoms improve (though arthropathy and endocrine damage may be irreversible). Routine screening of first-degree relatives of a confirmed case is recommended (iron studies ± genetic testing) to detect asymptomatic cases early.

Human homeostatic iron regulator protein, also known as the **HFE gene** (**H**igh **FE**2+)

- The Human homeostatic iron regulator protein regulates iron uptake into cells, when defective, the body absorbs excess iron

Table 3. Advice based on HFE genotype and serum ferritin

Genotype	Prevalence in Caucasian Australians[11,12]	Advice if serum ferritin is normal	Advice if serum ferritin is elevated
High risk HFE genotypes			
Highest risk C282Y homozygous	1 in 188	• Increased risk of future iron overload • Check iron studies every 1–5 years • Family members need testing[13]	• Begin venesections – candidate for therapeutic venesection • Family members need testing[13] • SF >1000 µg/L: refer to gastroenterologist, haematologist or physician with an interest in iron overload
Lower risk C282Y/H63D compound heterozygous	1 in 46		
Low risk HFE genotypes			
H63D homozygous	1 in 49	• Check iron studies every 1–5 years	• Not a candidate for therapeutic venesection but can become a volunteer blood donor if no contraindications exist • Look for another cause of elevated SF apart from HH, especially alcohol consumption, metabolic syndrome, obesity, liver disease and inflammation • Consider non-HFE haemochromatosis • Family members don't need testing[13] • SF >1000 µg/L: refer to gastroenterologist, haematologist or physician with an interest in iron overload
C282Y carrier H63D carrier No mutations	1 in 8 1 in 4 3 in 5	• No further follow up needed[13]	

Non-HFE Hereditary Hemochromatosis

- These are **rarer genetic forms** of primary iron overload, accounting for a small percentage of cases (often called Types 2, 3, and 4 HH).
- Non-HFE HH should be suspected if a patient has clinical iron overload (high ferritin *and* high transferrin saturation with organ involvement) but **no HFE mutations**. These cases are exceedingly rare; workup is always hepatology-led (liver biopsy and sometimes a Feriscan).
- For GPs, the key point is: **if it looks like haemochromatosis but HFE test is negative, refer to hepatology** for further evaluation.

Table 1 Genetic, clinical and laboratory features of the various types of Hereditary Haemochromatosis

HH Type	Gene	Inheritance	Clinical features	Laboratory findings	Liver pathology	Functional consequences of mutations
1	*HFE*	Autosomal recessive	May include: fatigue, lethargy, arthropathy, skin pigmentation, liver damage, diabetes mellitus, endocrine dysfunction, cardiomyopathy, hypogonadotropic hypogonadism	↑ serum ferritin, ↑ transferrin saturation	Hepatocyte iron loading, fibrosis, cirrhosis	Impaired hepcidin regulation by iron, leading to increased intestinal iron absorption and release of iron from reticuloendothelial cells
2A	*Hemojuvelin (HJV)*	Autosomal recessive	As for HFE. Earlier onset (< 30 yr). Cardiomyopathy and hypogonadism more prevalent.	↑ serum ferritin, ↑ transferrin saturation	Hepatocyte iron loading, fibrosis, cirrhosis	Loss of hepcidin regulation, leading to increased intestinal iron absorption and release of iron from reticuloendothelial cells
2B	*Hepcidin (HAMP)*	Autosomal recessive	As for HFE. Earlier onset (< 30 yr). Cardiomyopathy and hypogonadism more prevalent.	↑ serum ferritin, ↑ transferrin saturation	Hepatocyte iron loading, fibrosis, cirrhosis	No/inactive hepcidin, leading to maximal iron absorption and release of iron from reticuloendothelial cells
3	*Transferrin Receptor 2 (TfR2)*	Autosomal recessive	As for HFE.	↑ serum ferritin, ↑ transferrin saturation	Hepatocyte iron loading, fibrosis, cirrhosis	Impaired hepcidin regulation by iron, leading to increased intestinal iron absorption and release of iron from reticuloendothelial cells
4	*Ferroportin (Fpn), SLC40A1, IREG1, MTP1*	Autosomal dominant	Typical presentation: as for HFE, except generally milder. May have mild anaemia and lower tolerance to venesection.	↑ ↑ serum ferritin, normal transferrin saturation	Predominant Kupffer cell iron loading, fibrosis	Reduced ferroportin iron transport ability, leading to accumulation of iron in reticuloendothelial cells
			Atypical: as for HFE	↑ serum ferritin, ↑ transferrin saturation	Predominant hepatocyte iron loading, fibrosis, cirrhosis	Loss of ferroportin regulation by hepcidin, leading to increased intestinal iron absorption and release of iron from reticuloendothelial cells

Management of Hereditary Hemochromatosis

- **Goal of Therapy:** The primary treatment for HH is **iron removal by venesection (phlebotomy)**.
  - There is **no drug that increases iron excretion** as effectively for HH (iron chelators used only in specific circumstances)
- **Induction Phase:** The patient undergoes an “induction” phase of frequent venesection to deplete iron stores.
  - Typically, **500 mL of blood (≈250 mg iron) is removed weekly or fortnightly** until target iron levels are reached
  - The target is usually a **serum ferritin in the low-normal range (50–100 µg/L).**
  - It often requires removing several grams of iron; for example, removal of ~4 grams of iron without causing anaemia confirms substantial overload
- **Maintenance Phase:** Once ferritin is brought down to ~50 µg/L the patient enters a lifelong maintenance
  - The frequency of maintenance venesection is individualized, typically every **3 months** (quarterly) for many patients
  - The aim is to keep ferritin roughly between 50–100 µg/L.
  - GPs often take a larger role in maintenance
- **Role of GPs:** General practitioners play a crucial part in **monitoring and coordination**. While specialists usually initiate therapy and see the patient through induction, stable patients with HH may be co-managed with their GP. The GP should:
  - Ensure **regular ferritin and Hb checks** (e.g. every 3 months in maintenance, then adjust frequency).
  - Reinforce **lifestyle advice**: avoid excess dietary iron (no need for extreme iron avoidance, but avoid iron supplements), vitamin C supplements are not recommended in loading phase, moderate alcohol intake especially if liver disease.
  - Manage **associated conditions** (diabetes, arthropathy, hypogonadism) in collaboration with specialists.
  - Encourage **family screening**: advise that siblings of someone with genetic HH should have testing.

High Ferritin App

- **High Ferritin App (Lifeblood):** https://highferritin.transfusion.com.au
  - This web-based app allows doctors (including GPs) to refer patients for venesection at Lifeblood donor centres electronically
  - Patients will not be accepted for donation or therapeutic venesection with a history of HH without a referral
- **Eligibility**
  - Enter the patient's details, HFE genotype, and iron levels; the app's algorithm confirms if the patient meets criteria for Lifeblood therapeutic venesection (generally, confirmed or likely HH with elevated ferritin. **If eligible, it will generate a venesection schedule.**
  - If a patient has **high ferritin but no HFE mutation** or a non-hemochromatosis cause, the app will generally **decline therapeutic venesection.** In those cases, if venesection is still clinically indicated, it must be arranged via other avenues (hospital or QML/SNP). Alternatively, if the patient is otherwise healthy, the GP might encourage them to become a regular **volunteer blood donor** (donating blood every 3 months) which can incidentally help lower moderately elevated ferritin.
- **Wasted Blood**
  - Historical discussions about accepting HH patients as donors extended from concerns that those who benefit from donation through receiving treatment at no cost may not declare risk factors that would prevent them from donating.
  - Recent research by the Australian Red Cross Lifeblood service (2024) revealed that approximately 73,000 bags of blood are being discarded each year in Australia due to therapeutic venesections done outside the Lifeblood system
  - HH patients already contribute significantly: they constitute about 2.5% of Australia's blood donor panel (around 15,000 donors making 37,000 donations per year)
  - Those with HH can donate both red cells and plasma, see: https://onlinelibrary.wiley.com/doi/10.1111/trf.13802 and https://www.lifeblood.com.au/news-and-stories/media-centre/media-releases/dont-bin-your-blood

Case Study 2

- **Scenario:** A 36-year-old man visits his GP with **fatigue** and **erectile dysfunction**. He also has increased skin pigmentation on his forearms (“I seem to tan even without sun”) and was recently found to have new-onset **type 2 diabetes**. Family history reveals his brother has “some liver issue” (unknown specifics). He has been using 1 ferro-grad C tablet second daily for 4 months in an attempt to manage his fatigue.
- **Examination:** He has a bronzed skin tone. No signs of chronic liver disease (no ascites, jaundice, no spider nevi). There is some lower limb peripheral oedema. The examination is otherwise normal.
- **Investigations:**
  - **FBC:** platelet count 180, otherwise normal
  - **UEC:** normal
  - **TSH:** normal
  - **CRP:** normal
  - **Iron studies:** Ferritin **2,020 µg/L** (very high); Transferrin saturation **82%** (markedly elevated).
  - **Liver enzymes:** Bilirubin 8µmol/L, Albumin 37 g/L, ALT 55 U/L, AST 56 U/L (near upper limit of normal, slight elevation)
  - **Fasting glucose:** 12 mmol/L (elevated; consistent with diabetes). HbA1c 7.0%.
  - **HFE genetic test: no mutations detected**.
  - **CT Chest, Abdomen and Pelvis:** Hepatic steatosis, no other significant findings.

Case Study 2

- **MCQ1: Which of the following is NOT a test required to assess for complications of hereditary haemochromatosis?**
  a) Ultrasound Liver and either Shear wave elastography or Fibroscan
  b) Serum Testosterone
  c) ECG (and/or TTE and CXR)
  d) Serum creatinine

- **MCQ2: What is the most appropriate next step in management for this patient?**
  a) Advise the patient to reduce dietary iron intake sharply and recheck labs in 6 months
  b) Refer to a hepatologist to initiate venesection therapy and further workup
  c) Therapeutically phlebotomize 1 unit of blood in the GP clinic and follow up weekly
  d) Refer the patient to Lifeblood for venesection

Case Study 2

- **Group Discussion:** What is going on here
  - What could the diagnosis be?
  - Would you refer to hepatology?
  - What would you do apart from referring to hepatology?
  - How do we go about managing the complications?

Case Study 3

- **Scenario:** Jane is a 55-year-old woman who was diagnosed with HFE-haemochromatosis (C282Y homozygote) through family screening. Her ferritin at diagnosis was 600 µg/L with transferrin saturation 70%. She has no signs of organ damage (caught early, ferritin normal). She underwent an induction course of therapeutic venesection at a hospital clinic – **one 500 mL phlebotomy every two weeks for 16 weeks** – which brought her ferritin down to 50 µg/L with a haemoglobin of 135 g/L. She tolerated the procedures well.
- **Current Status:** Now that Jane's iron stores are depleted, she is ready to transition to **maintenance therapy**. Jane is sick of driving to the hospital and refuses to return due to the cost of parking. The specialist calls you and suggests venesection through Lifeblood. Jane is otherwise healthy and keen to have her blood used for donations if possible.
- **At the GP Clinic:** You decide to use the **Lifeblood High Ferritin App** to facilitate her maintenance therapy. The app approves her for therapeutic donation and suggests a **maintenance schedule** of one venesection **every 3 months.** Jane will now have her blood removed at the local Lifeblood donor center. You plan to check her ferritin and transferrin saturation every 3 months initially to fine-tune this interval.

Default Therapeutic Venesection Schedule: 3 Monthly venesection - No Review Required

Program	Ferritin	Schedule	Review of Schedule Required
1	> 1000	Weekly	10 Weeks
2	500 - 1000	Weekly	5 Weeks
3	200 - 499	4 Weekly	3 Months
4	50 - 199	3 Monthly	Not Req*
5	< 50	3 Monthly [1]	Not Req*

[1] - *This patient does not have iron overload but may attend three monthly for maintenance venesection. Please monitor your patient's ferritin. If ferritin drops below 25 cease venesection.*

*not req** - *Unless increased frequency or change in medical status*

Case Study 3

- **MCQ1: After 12 months of 3 monthly venesections, her last two ferritin results have been 105 and then 120. What would you do?**
  a. No further venesection needed unless symptoms recur – her ferritin is in normal range now
  b. Return to venesecting weekly
  c. Return to venesecting fortnightly
  d. Schedule maintenance venesection every 2 months

- **MCQ2: What is the MOST likely reason Jane presented with a ferritin <1000 and no end organ damage so late in life?**
  a) The presence of the C282Y/C282Y genotype
  b) A diet high in green leafy vegetables
  c) Female gender
  d) Proton Pump Inhibitor use for 5 years

Key Takeaways

- Most raised ferritin in primary care is due to alcohol use and metabolic causes (MASLD/metabolic syndrome), not iron overload
- Think transferrin saturation first: TS ≥45% suggests iron overload; TS ≥55% is more specific; TS <45% makes significant iron overload unlikely
- Alcohol clues: high GGT, AST>ALT, macrocytosis; try 6–8 weeks abstinence and repeat ferritin to confirm contribution
- Initial workup: repeat fasting iron studies with CRP, FBC, LFTs, hepatitis B and C serology, metabolic risk profile; consider thyroid tests; liver ultrasound if LFTs are elevated
- Do not start venesection until true iron overload is confirmed
- Refer if ferritin >1000, there is suspected or confirmed iron overload, organ damage, or an unclear cause after appropriate workup; ferritin >3000 micrograms per litre warrants urgent telephone discussion
- The vast majority who develop the Hereditary haemochromatosis clinical syndrome are C282Y/C282Y homozygotes; compound heterozygotes usually have a modifiable cofactor and only occasionally require venesection, with end organ dysfunction uncommon

Community HealthPathways
Brisbane North
Lifestyle and Preventive Care
Medical
Assault or Abuse
Cardiology
Dermatology
Diabetes
Endocrinology
Gastroenterology
Acute Abdominal Pain in Adults
B12 Deficiency
Bowel Cancer Screening
Chronic Abdominal Pain in Adults
Bowel Polyp Surveillance
Coeliac Disease in Adults
Colorectal Symptoms
Constipation in Adults
Diarrhoea in Adults
Dysphagia
Dyspepsia and GORD
Enteral Feeding Tubes in Adults
Inflammatory Bowel Disease (IBD)
Irritable Bowel Syndrome (IBS)
Liver Conditions
Abnormal Liver Function Tests
Fatty Liver
Hepatitis B
Hepatitis C (HCV)
Hereditary Haemochromatosis and Raised Ferritin
Incidental Liver and Spleen Lesions
Gastroenterology Requests

Hereditary Haemochromatosis and Raised Ferritin

This pathway is about hereditary haemochromatosis, and is not a comprehensive work up of other causes of raised ferritin.

Background

About hereditary haemochromatosis (HH) and raised ferritin

Assessment

1. Consider screening for haemochromatosis if:
   - family history of HH.
     - First-degree relative – arrange fasting iron studies, and HFE gene testing for C282Y and H63D mutations (less common mutations are not routinely checked).
     - Second-degree or more distant relative – arrange fasting iron studies.
   - incidental finding of raised ferritin.
     - Allow any acute illness to resolve.
     - Consider other investigations as appropriate to exclude other causes of raised ferritin.
   - features suggestive of HH.
     - Many patients with HH will be asymptomatic. Symptoms may appear between ages 30 to 60 years, with women generally presenting after menopause.
     - Arrange fasting iron studies, as well as tests appropriate to the presenting symptoms and signs.
   - incidental finding [1] on full blood count (FBC) of mean corpuscular volume (MCV) > 94 fL, or mean cell haemoglobin. (MCH) > 32.2 pg – arrange fasting iron studies, and E/LFTs.
   - abnormal liver function tests where the cause has not been established – arrange fasting iron studies.
2. Check iron studies:
   - Transferrin saturation:
     - Iron supplements will cause a raised transferrin saturation. If the patient was taking iron supplements at time of testing, consider repeating iron studies after the patient has been off iron for at least 48 hours.
     - A value of ≥ 45% suggests iron overload – arrange HFE gene testing.
   - Raised ferritin:
     - Ferritin moderately raised (< 1000 micrograms/L) and transferrin < 45%
     - Ferritin moderately raised (< 1000 micrograms/L) and transferrin ≥ 45%
     - Ferritin ≥ 1000 micrograms/L
3. Check HFE gene testing results:
   - Homozygous (C282Y) and compound heterozygous (C282Y/H63D) each confirm HH and explain raised ferritin.
   - Other results (e.g., heterozygous C282Y (a carrier) or homozygous H63D) do not usually indicate HH. Consider other causes of raised ferritin.
   - A few patients with HH do not have the commonly checked HFE gene mutations, and a liver biopsy may be required for diagnosis.

Queensland Government | Smart Referrals

Dr Fred Findacure

Patient name: Nicole METRONORTH DoB: 29 Sep 1977

Request information

Request date	21 Oct 2025
* Request type	New referral | Update | Continuation | Request for advice
* Reason for referral	(•) New condition requiring specialist consultation ( ) Deterioration in condition, recently discharged from outpatients < 12 months ( ) Other
* Priority	Urgent | Routine
* Provider	QHSR | Private

Consents

* Date patient consented to request	21 Oct 2025
* Patient is willing to have surgery if required?	Yes | No | Not applicable
* Condition and Specialty	Gastroenterology - Elevated iron studies (Hepatology) (Adult) HealthPathways
Suitable for Telehealth?	Yes | No
* Are you the patient's usual GP?	Yes | No

Request recipient

* Service/Location	Please select
Specialist name	
Organisation details	

Hepatology	ROYAL BRISBANE & WOMEN'S HOSPITAL	6.4 km	
Hepatology	THE PRINCE CHARLES HOSPITAL	12.2 km	
Hepatology	REDCLIFFE HOSPITAL	31.5 km	
Hepatology	PRINCESS ALEXANDRA HOSPITAL	1.8 km	Out of catchment

Condition specific clinical information +

Investigations and imaging +

Standard clinical information +

Patient information +

Insurance information +

Elevated iron studies

Emergency department referrals

All urgent cases must be discussed with the on call Registrar to obtain appropriate prioritisation and treatment. Contact through:

- Royal Brisbane and Women's Hospital (07) 3646 8111
- The Prince Charles Hospital (07) 3139 4000
- Redcliffe Hospital (07) 3883 7777
- Caboolture Hospital (07) 5433 8888

Urgent cases accepted via phone must be accompanied with a written referral and a copy faxed immediately to the Central Patient Intake Unit: 1300 364 952.

Potentially life-threatening symptoms suggestive of:

- Acute severe GI bleeding
- Acute liver failure: (acutely abnormal liver blood tests in absence of cirrhosis, associated with development of coagulopathy and hepatic encephalopathy)
- Sepsis in a patient with cirrhosis
- Severe encephalopathy in a patient with liver disease
- New significant renal dysfunction in a patient with cirrhosis

Does your patient wish to be referred?

Minimum referral criteria

Does your patient meet the minimum referral criteria?

Category 1
Appointment within 30 days is desirable

- Evidence of iron overload with liver decompensation (e.g. jaundice and/or ascites and/or encephalopathy)

Category 2
Appointment within 90 days is desirable

- Elevated serum ferritin level **without** presence of concerning features

Category 3
Appointment within 365 days is desirable

- Normal ferritin with positive HFE gene study (e.g. C282Y homozygosity or compound heterozygosity (C292Y/H63D))

If your patient does not meet the minimum referral criteria

Consider other treatment pathways or an alternative diagnosis.

If you still need to refer your patient:

- Please explain why (e.g. warning signs or symptoms, clinical modifiers, uncertain about diagnosis, etc.)
- Please note that your referral may not be accepted or may be redirected to another service

+ Other Hepatology conditions

Send referral

Hotline: 1300 364 938

Electronic:
GP Smart Referrals (preferred)
eReferral system templates
Medical Objects ID: MQ40290004P
HealthLink EDI: qldmnhhs

Mail:
Metro North Central Patient Intake
Aspley Community Centre
776 Zillmere Road
ASPLEY QLD 4034

Health pathways

Access to Health Pathways is free for clinicians in Metro North Brisbane.

For login details email:
healthpathways@brisbanenorthphn.org.au

Login to Brisbane North Health Pathways:
brisbanenorth.healthpathwayscommunity.org

Locations

Caboolture Hospital
Redcliffe Hospital
Royal Brisbane and Women's Hospital
The Prince Charles Hospital

Resources

Specialists list
General referral criteria