



High Ferritin and Iron Overload – Investigation and Management

DRAFT: For External Review

Effective Date: TBD

Scope

This guideline provides recommendations for the investigation and management of high ferritin levels (also known as hyperferritinemia) in out-patient adults aged > 19 years. The objectives are to differentiate underlying causes and identify those which require intervention to reduce iron overload.

Diagnosis and management of hereditary hemochromatosis (HH) due to mutations in the *HFE* (High FE) gene (referred to as *HFE*-associated hereditary hemochromatosis; *HFE*-HH) is included. Equipment and procedures for therapeutic phlebotomy are outlined. Cascade testing of family members of patients with *HFE*-HH is included. Hemochromatosis caused by mutations in iron-related genes other than *HFE* is outside the scope of this guideline.

Because the non-*HFE*-HH causes of hyperferritinemia are so diverse, their management is out of scope. They should be managed according to the underlying condition.

Key Recommendations¹

- High ferritin levels are most commonly caused by inflammation, infection, liver disease (particularly non-alcoholic steatohepatitis (NASH)/fatty liver), renal disease, alcohol excess, metabolic syndrome or malignancy. In these cases, a high ferritin level does not accurately reflect iron stores.¹
- The first-line investigations for a patient with a raised serum ferritin are:
 - **History taking:** family history of iron overload, alcohol intake and other risk factors for liver disease, transfusion history, type 2 diabetes mellitus, obesity, hypertension, and symptoms and signs of an underlying inflammatory or malignant disorder.
 - **Lab tests:** repeat serum ferritin, transferrin saturation (TSAT), complete blood count and peripheral smear, serum creatinine and electrolytes, liver enzymes (ALT and GGT) with consideration of viral hepatitis screening and abdominal ultrasonography (if suspected liver disease or elevated liver enzymes), and blood glucose and lipid studies, if not recently performed.
- Testing for *HFE*-HH is not recommended in patients of non-European ancestry because its prevalence is very rare.
- East Asians have ferritin values 1.5-2x higher than the reference norms reported.
- Iron overload can generally be excluded when TSAT <45%.

¹ The key recommendations are adapted from the British Journal of Hematology Guideline *Investigation and management of a raised serum ferritin* and adapted to the BC primary care context.

Definitions and Clinical Context

Hyperferritinemia is commonly detected incidentally, or purposely, when ferritin is ordered to:

- screen for iron deficiency in patients complaining of fatigue (refer to [BC Guideline: Iron Deficiency – Diagnosis and Management](#))
- investigate the causes of microcytic anemia
- screen for iron overload (addressed herein)

Hyperferritinemia: occurs when a patient’s serum ferritin is above the upper reference interval. The upper reference interval varies with age, gender, and laboratory method. East Asians have ferritin values 1.5-2x higher than the reference norms reported.² Refer to [Appendix A](#) for ferritin laboratory values and comments.

Because ferritin is an acute phase reactant, hyperferritinemia is most commonly caused by inflammation, infection, liver or renal disease, or malignancy. In these cases, a high ferritin level does not accurately reflect iron stores and does not rule out iron deficiency or indicate iron overload, as the ferritin protein is released from macrophages irrespective of iron content. Although much less frequent, hyperferritinemia is also caused by an excess of iron stores or iron overload.

Extreme hyperferritinemia >3000 µg/L can be seen in transfusional iron overload, severe liver disease, hemophagocytic syndromes, renal failure, sepsis, and other severe illnesses, typically in a hospital setting.

In patients with serum ferritin levels >10,000 µg/L, acute hepatitis and rare conditions such as adult onset Still disease, hemophagocytic lymphohistiocytosis and haematological malignancies should be considered.

Iron overload: occurs when iron absorption exceeds physiological requirements, leading to excess stores. This is indicated by TSAT \geq 45% and can occur from:

- Transfusion-dependent anemias (e.g. sickle cell anemia)
- Anemia from ineffective erythropoiesis (e.g. thalassemia, myelodysplastic syndrome)
- Chronic liver diseases (e.g. viral hepatitis, NASH, fatty liver)
- Chronic excessive ingestion of medicinal iron
- Hereditary hemochromatosis (HH)

HFE-associated Hereditary Hemochromatosis (HFE-HH): is an autosomal recessive genetic disorder common in individuals of European ancestry, in which an increase in the intestinal absorption of iron leads to excessive iron deposits in organs such as liver, pancreas, heart, pituitary, testicles, joints, and skin. Early detection and treatment can completely prevent clinical sequelae, and, in symptomatic patients, phlebotomy effectively reduces morbidity and mortality.^{3,4}

HFE-HH has a relatively low clinical penetrance, with fewer than 10% of those homozygous for the C282Y variant (the most common mutation) developing clinical manifestations,⁵ mainly in the form of hepatic iron overload. Clinical manifestation (see Table 1) usually develops by age 40-50 in men and age 50-60 in women.

Over 80% of HFE-HH is due to homozygous mutation for C282Y in the HFE gene.^{3,4} Hemochromatosis caused by mutations in other iron-related genes are rare and are outside the scope of this guideline.⁶ Suspected cases should be referred to a specialist. Information on the epidemiology of HFE-HH is provided in [Appendix A: Epidemiology of HFE hemochromatosis](#).

Signs and Symptoms

► Signs and symptoms of high ferritin levels

The signs and symptoms of high ferritin are due to the underlying conditions and not to the high ferritin in and of itself.

► Signs and symptoms of iron overload

Iron overload is often missed because its symptoms are nonspecific and gradual multiorgan damage occurs over many years. Its symptoms can be confused with those of much more common diseases, such as alcoholic liver disease, diabetes, and osteoarthritis. If untreated, iron overload can cause serious organ damage and premature death.

Table 1. Signs and symptoms of iron overload by organ

Iron Storage	Consequences
Liver	Enlargement, progressing to cirrhosis and predisposing to hepatocellular carcinoma
Heart	Congestive heart failure and/or arrhythmia due to cardiomyopathy
Pancreas	Diabetes - difficult to control type 2 or atypical presentation (e.g. young, low BMI)
Skin	Increased skin pigmentation (“bronze”); association with porphyria cutanea tarda
Hair	Hair loss
Joints	Arthritis, classically involvement of MCP and proximal IP joints of thumb, index and middle fingers; chondrocalcinosis
Pituitary	Hypogonadism and hypothyroidism
Testes	Hypogonadism

Most patients with clinical hemochromatosis develop only one or a few of the above problems, with liver involvement and enlargement being the most common, occurring in most affected patients. Patients are often not diagnosed until aged > 40 years in males and > 50 years in females because clinical findings are uncommon before that age. However, nonspecific symptoms such as arthralgias, fatigue, and abdominal pain may be noted years before organ dysfunction becomes apparent.

Significant end-organ damage is rare with a ferritin value < 600 µg/L. The routine complete blood count (CBC) is typically normal in hemochromatosis. Iron overload does not cause high hemoglobin.

Diagnosis

► Differential diagnosis of high ferritin

Reactive causes of high ferritin, including inflammatory disorders, liver disease (particularly non-alcoholic steatohepatitis (NASH)/fatty liver), alcohol excess, malignancy, renal failure, and

metabolic syndrome are each more common than hemochromatosis.¹ Fatty liver is a very common cause of high ferritin in out-patients.

Table 2. Causes of raised serum ferritin (adapted from Table 1, Cullis 2018¹)

Increase in ferritin synthesis not associated with significant iron accumulation	Increased ferritin as a result of cellular damage	Increased ferritin synthesis due to iron accumulation
<ul style="list-style-type: none"> • Acute and chronic infection • Chronic inflammatory disorders • Autoimmune disorders • Malignancies • Malignant or reactive histiocytosis • Hereditary hyperferritinemia with and without cataracts • Gaucher disease 	<ul style="list-style-type: none"> • Chronic excess alcohol consumption • Liver diseases including: liver failure, chronic viral hepatitis, alcoholic and non-alcoholic steatohepatitis² 	<ul style="list-style-type: none"> • Hereditary hemochromatosis • Secondary iron overload from blood transfusion or excessive iron intake/administration • Ineffective erythropoiesis: sideroblastic anemia, some myelodysplastic syndromes (e.g. refractory anemia with ring sideroblasts) • Thalassemia • Other rare genetic disorders

► History taking

Key questions to ask in a patient with raised serum ferritin levels:

1. Extent of alcohol intake
2. Risk factors for viral hepatitis (e.g., travel, high risk activities such as intravenous drug use)
3. Signs and symptoms or known inflammatory condition (e.g., rheumatoid arthritis)
4. Signs and symptoms or known malignancy
5. Diabetes mellitus and risk factors
6. Metabolic syndrome (hypertension, diabetes, obesity)
7. History of blood transfusions, specifically, frequency and duration of red cell or whole blood transfusion
8. Family history of iron overload, hemochromatosis, anemia, hemoglobinopathies or other hematological conditions

► Initial laboratory investigations

- If the serum ferritin is elevated and there is a potential transient cause (e.g., acute infection, flare of a chronic inflammatory condition), recheck the serum ferritin no sooner than one week after the transient cause has resolved.
- Unless recently investigated, the following tests are recommended for patients with a

² May also have iron overloading.

persistently elevated, otherwise unexplained, serum ferritin level:

- TSAT
 - CBC with peripheral smear
 - serum creatinine
 - ALT and GGT: if elevated, investigate for common causes of hepatitis (e.g. viral, NASH, alcohol)
 - abdominal ultrasound if clinical suspicion for liver disease or liver enzymes are elevated
 - glucose and HbA1C
 - lipid studies: triglycerides and non-HDL cholesterol
- If TSAT <45%, then iron overload is generally excluded.
 - If TSAT \geq 45%, then investigations for causes of iron overload, particularly for *HFE*-HH in those of European descent (see below), should proceed if there is no history of multiple transfusions or excessive medicinal iron intake.
 - *HFE*-HH testing is not recommended for East and South Asian individuals, or those of other non-European ancestries, because *HFE*-HH is extremely rare in these groups. Further information on non-indications for testing *HFE*-HH is provided in [Appendix C: Whom not to perform genetic testing for *HFE*-HH](#).

► Investigations to determine degree of iron overload

In some cases, patients may need additional testing to confirm or rule out iron overload, which may include MRI of the heart or liver. This is usually arranged by a specialist and the specific MRI protocols to assess for iron are not widely available.

Testing for *HFE*-HH

► Indications for testing

Genetic testing for *HFE*-HH is indicated in patients of European descent with a persistently elevated serum ferritin AND TSAT \geq 45%. The tests that the laboratory will perform for each indication are described in [Appendix D: Laboratory Test Procedures for *HFE*-HH Testing](#), the patient can go to any collection laboratory.

► Patients previously treated for *HFE*-HH where the genetic test result is unavailable

Individuals who have previously been treated for hemochromatosis should be offered genetic testing if not already performed. For ordering guidance, see Division of Genome Diagnostics webpage (www.genebc.ca) under frequently asked questions.

► Completing the standard outpatient laboratory requisition

The following table outlines the appropriate settings for testing for *HFE*-HH and how to fill out the laboratory requisition. **Checking the specific categories in the laboratory requisition facilitates appropriate genetic testing.**

Table 3. Indications for *HFE*-HH testing and instructions for filling out the laboratory requisition

Indication for <i>HFE</i> -HH Genetic Testing	How to fill out the standard out-patient laboratory requisition ³
Testing for patients with clinical features of iron overload	
Individuals of European ancestry with raised ferritin and TSAT $\geq 45\%$	Under <i>HFE</i> -Hemochromatosis, check off “Confirm diagnosis”
Cascade testing for a patient with family history of hemochromatosis	
Patient has a child with C282Y;C282Y <i>HFE</i> genotype	Under <i>HFE</i> -Hemochromatosis, check off “Confirm diagnosis”
Adult patient with family history of hemochromatosis (genotype of relative is unknown or not <i>HFE</i> C282Y;C282Y)	
Adult patient’s sibling or parent has confirmed C282Y;C282Y <i>HFE</i> genotype	Under <i>HFE</i> -Hemochromatosis, check off “Sibling/parent is C282Y/C282Y homozygote”
Patient < 19 years old with family history of hemochromatosis	See Appendix C: Whom not to perform testing for <i>HFE</i>-HH

Interpreting Results from *HFE*-HH Testing

► Patients homozygous for *HFE* C282Y (C282Y;C282Y)

Patients with hyperferritinemia, TSAT $\geq 45\%$ and genetic testing confirming C282Y homozygosity have a diagnosis of *HFE*-HH. Most will require reduction of their iron stores with a phlebotomy program (see [Appendix E: Management and surveillance of *HFE*-HH](#)). Good phlebotomy technique is important for maintaining venous access long term (see [Appendix F: Therapeutic Phlebotomy Using an 18 Gauge Cannula](#)). Prior to initiating a phlebotomy program, the patient should be thoroughly assessed for possible end organ damage (e.g., arthritis, liver dysfunction, diabetes, heart disease). Patients with ferritin > 1,000 $\mu\text{g/L}$ should have liver function tests because of the increased risk of cirrhosis and hepatoma.⁷ Management and surveillance of patients with a diagnosis of *HFE*-HH are provided in [Appendix E: Management and surveillance of *HFE*-HH](#).

► Patients heterozygous for *HFE* C282Y

Patients heterozygous for *HFE* C282Y are most often asymptomatic carriers. However, they may have a clinical phenotype of hereditary hemochromatosis due to co-inheritance of other genetic

³ The standard out-patient laboratory requisition (SOPLR) is available from: gov.bc.ca/assets/gov/health/forms/1901fil.pdf

factors (e.g., another mutation in the same gene, or a co-inherited mutation in another gene), and/or other comorbidities (e.g., alcohol use disorder, hepatitis C).⁸ If the clinical phenotype strongly suggests hereditary hemochromatosis, refer to a specialist to consider hepatic iron studies and/or additional genetic investigations.

Indications for Specialist Referral

The following patients should be referred to a specialist (i.e., general internist, gastroenterologist/hepatologist or hematologist) for further investigations or management:

- *HFE*-HH with organ dysfunction or damage (e.g., cirrhosis, heart failure)
- Absence of C282Y/C282Y homozygosity, including heterozygous for *HFE* C282Y, with serum ferritin > 1,000 µg/L and TSAT ≥45% or clinical features of iron overload
- Unexplained persistent serum ferritin > 1,000 µg/L, with or without clinical or laboratory evidence of iron overload (see Table 2)

► Recommended history and tests to include in referral package

History containing clinical features suggestive of iron overload and results from first line investigations indicated above. Genetic studies and family history should be included if available.

► Please use for referral:

- Use [Pathways](#) to see the list of specialists in your region and their wait times.
- Real-time communication with local specialists (or RACE Line if uncertain) can provide rapid advice for urgent cases and facilitate the most appropriate mechanism of referral.

Resources

► Practitioner Resources

- BC Children’s Hospital and BC Women’s Hospital Division of Genome Diagnostics: <http://genebc.ca/>

► Patient, Family and Caregiver Resources

- HealthLink BC: <https://www.healthlinkbc.ca/health-topics/hw180388>
- Canadian Hemochromatosis Society: <https://www.toomuchiron.ca/>
- Canadian Blood Services – Information about blood donation for individuals with hemochromatosis: blood.ca/en/blood/am-i-eligible/abcs-eligibility/hemochromatosis

How this guideline was developed

This guideline was adapted from the British Journal of Hematology Guideline *Investigation and management of a raised serum ferritin*.¹ We used the [ADAPTE process](#) (Guidelines International Network, 2010) to adapt the recommendations to the BC primary care context. We added guidance on diagnosis and management of hereditary hemochromatosis, based on the BC Guideline *HFE-Associated Hemochromatosis Investigations and Management* (2013).

For more information about how BC Guidelines are developed, please refer to the [GPAC Handbook](#).

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Diagnostic Codes

- 257.0 Disorders of iron metabolism
- 275.01 Hereditary hemochromatosis
- 275.02 Hemochromatosis due to repeated red blood cell transfusions

- 275.03 Other hemochromatosis
- 275.09 Other disorders of iron metabolism

▶ **Appendices**

- [Appendix A: Laboratory values and comments on ferritin testing](#)
- [Appendix B: Epidemiology of HFE hemochromatosis](#)
- [Appendix C: Whom not to perform genetic testing for HFE-HH](#)
- [Appendix D: Laboratory test procedures for HFE-HH Testing](#)
- [Appendix E: Management and surveillance of HFE-HH](#)
- [Appendix F: Therapeutic phlebotomy using an 18 gauge cannula](#)

▶ **Associated Documents**

- [BC Guideline: Iron Deficiency – Investigation and Management](#)
- [BC Guideline Ultrasound Prioritization](#)
- [BC Guideline: C-Reactive Protein and Erythrocyte Sedimentation Rate Testing](#)
- BC Guideline: Hepatitis Testing (in development)

Appendix A: Laboratory Values and Comments on Ferritin Testing

The following updated ranges are undergoing review and are currently not included on BC lab reports.

Elevated ferritin result (ug/L)	Lab report comment
200 - <400	Ferritin results under 400 ug/L generally do not require further investigation. For more information see BCGuidelines.ca
400 – 600*	Mild elevations in ferritin are most frequently an acute phase reaction. For more information see BCGuidelines.ca
>600*	Significant elevations in ferritin may indicate iron overload. For more information see BCGuidelines.ca

*results above 400 ug/L will be flagged as an abnormal result in the laboratory report

Appendix B: Epidemiology of HFE hemochromatosis

HFE-HH is the most common genetic disorder in the western world. Approximately 1 in 300 individuals of European ancestry are homozygous for the C282Y *HFE* gene variant⁸ (i.e., both copies of the *HFE* gene carry this genetic change) and 1 in 9 such individuals are carriers (see Table 2). *HFE*-HH is rare in individuals of other ancestries, including East and South Asians, largely due to the rarity of the C282Y variant in these non-European populations.⁹

Table 1. Estimated number of people with *HFE* C282Y in the BC population based on the Canadian 2016 Census¹⁰

Genotype	Estimated # individuals in BC
Homozygote (C282Y;C282Y)	7846
Heterozygote	362,622

Table 2. *HFE*-HH-C282Y in different populations⁸

Population	Homozygote frequency (%)	Carrier Frequency (%)
European	0.33	11.0
Latino	0.02	2.7
African	0.01	2.1
South Asian	~0	0.4
East Asian	~0	0.03

Appendix C: Whom not to perform genetic testing for *HFE*-HH

► The following scenarios do not warrant genetic testing for *HFE*-HH:

- Screening the general population.
- Testing individuals of non-European descent for *HFE*-HH as the C282Y variant is exceedingly rare in the non-European population; thus, a negative *HFE*-HH genetic test has no clinical utility. See Appendix B: Epidemiology of *HFE* hemochromatosis for the prevalence of hereditary hemochromatosis in different populations. Non-European patients with evidence of iron overload (persistently high ferritin AND TSAT $\geq 45\%$) should be referred to a specialist.
- Patients with clinical findings that are found in iron overload but who do not have a TSAT $\geq 45\%$.
- Children (< 19 years of age) not competent to decide for themselves whether they want the information. As *HFE*-HH is an adult-onset disorder, genetic testing is not generally indicated in children and so can be deferred until the child is able to exercise autonomy regarding decision making.^{11,12}
- Parents of individuals homozygous for C282Y (i.e. C282Y;C282Y genotype) who do not themselves have hyperferritinemia and a TSAT >45%.
- First-degree relatives (parents, siblings and children) of individuals identified to be heterozygous for C282Y (whether carrier or compound heterozygote) who do not have hyperferritinemia and a TSAT >45%.
- First-degree relatives (parents, siblings and children) of individuals with non-C282Y *HFE* genotypes who do not themselves have hyperferritinemia and a TSAT >45%.¹³

Appendix D: Laboratory Test Procedures for *HFE*-HH Testing

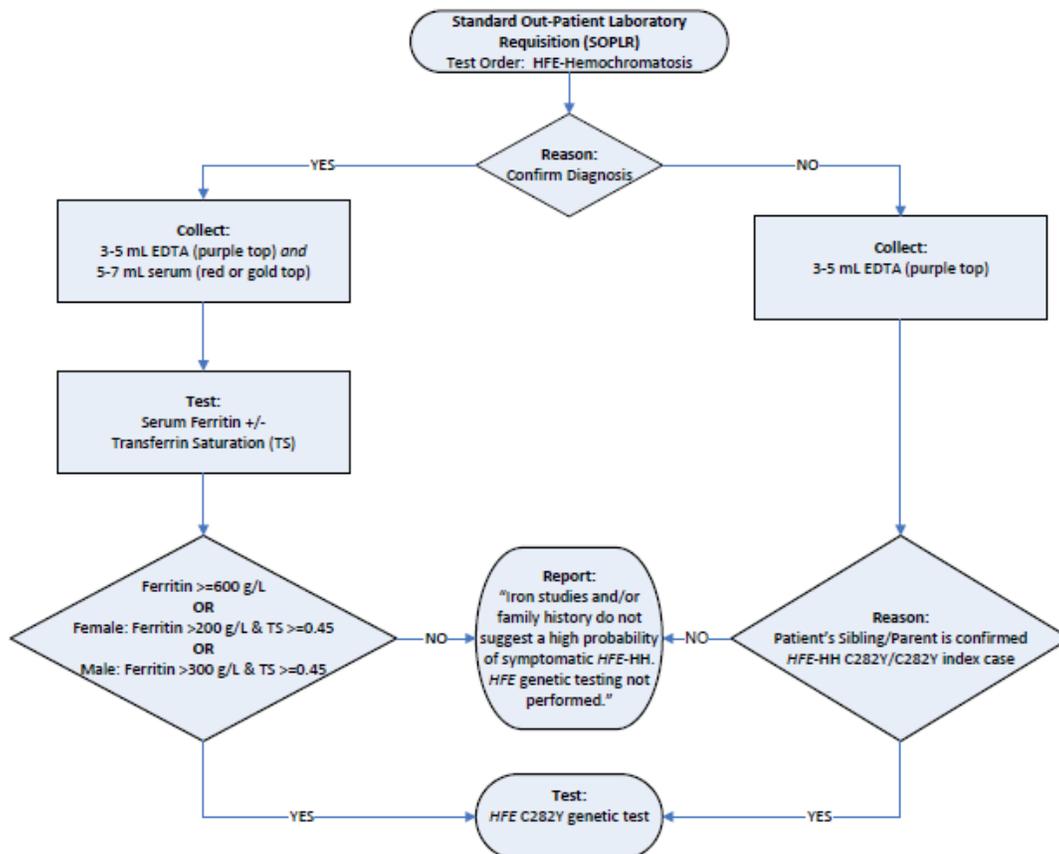
This Appendix outlines the testing the laboratory will perform based on the requisition. Refer to Table 3 on page 6 for the indications for testing and associated instructions for filling out the requisition.

In all cases, the laboratory will collect an EDTA sample for *HFE* C282Y genetic testing and, where applicable, a serum sample for serum iron studies (serum ferritin, serum transferrin, TIBC).

- A. For those presenting with symptoms and signs of hemochromatosis, or with persistently elevated ferritin levels, or with a family history of hemochromatosis (genotype of relative unknown or not C282Y;C282Y), the results of the serum iron studies will determine whether or not genetic testing will be done (see Figure 1 below).
- B. Siblings and children of individuals with confirmed *HFE*-HH due to C282Y homozygosity (i.e., genotype C282Y; C282Y) will not have iron studies performed prior to genetic testing (see Figure 1).

Note: Requests for ferritin and/or TSAT do NOT constitute requests for *HFE*-HH testing.

► Figure 1: Hemochromatosis Test Procedure



Appendix E: Management and surveillance of *HFE*-HH

▶ Therapeutic Phlebotomy

- Phlebotomy is the treatment of choice for hemochromatosis and for other primary iron overload disorders. Possible exceptions include those who are already anemic or have limited life expectancy due to other diseases or those with congestive heart failure with hemodynamic instability.
- Volume and frequency of phlebotomy need to be individualized according to the patient's age and clinical and biochemical presentation. Most patients will not tolerate phlebotomy more frequently than every 2 – 4 weeks and smaller volumes may be indicated in women. Guidelines recommend that for severely iron overloaded patients, weekly phlebotomy of 500 ml of whole blood should be continued until serum ferritin is 50-100 µg/L, within the patient's tolerance. Consider venous access, frequency of phlebotomy, and symptoms of iron deficiency). Patients with massive iron overload may require in excess of 100 phlebotomies.
- Serum ferritin and hemoglobin should be monitored regularly (e.g., every 4th phlebotomy) to assess response to therapy. It is unusual for iron overloaded patients to develop anemia early in the course of phlebotomy therapy. If this occurs, reduce the frequency of phlebotomy.
- Once patients have been successfully depleted of excess iron stores (ferritin <50 µg/L), a program of monitoring and maintenance should be established. The need for maintenance phlebotomy is quite variable; some patients require phlebotomy every 2 - 4 months to maintain a low-normal ferritin, and some may not re-accumulate for many years.
- At minimum, the CBC and ferritin should be checked every 12 months, and phlebotomy should be re-initiated if the ferritin is rising toward the upper limit of normal.
- People with hemochromatosis can donate blood, providing they meet all other Canadian Blood Services donor eligibility criteria. Individuals with late complications from hemochromatosis such as liver cirrhosis or heart failure are not eligible to donate. See details from Canadian Blood Services at: blood.ca/en/blood/am-i-eligible/abcs-eligibility/hemochromatosis

▶ Chelation

- Although iron can be pharmacologically removed using chelating agents such as deferasirox and desferrioxamine, these are rarely used and should be reserved for patients who are unable to tolerate phlebotomy (i.e., patients with chronic anemia due to thalassemia major, myelodysplastic syndromes, etc.).
- Phlebotomy is safe and cost-effective and thus the preferred modality of iron removal for patients able to tolerate it.

▶ Organ Damage

- In patients with organ damage, such as cirrhosis, congestive heart failure, hypogonadism, referral to the relevant specialist is recommended.
- End organ damage should be reassessed periodically. Reversal of organ impairment is sometimes seen once iron stores have been depleted. For example, if liver enzymes have been abnormal, they often improve with phlebotomy. There may also be improvement in iron-induced cardiac dysfunction. Diabetic patients often note improvement in blood sugars with less dependency on insulin or oral hypoglycemic agents. Conditions that often do not improve with phlebotomy include arthropathy, cirrhosis and testicular atrophy.

▶ **Dietary Restriction**

- Strict avoidance of dietary iron is not necessary, but iron and vitamin C supplements should be avoided.¹⁴ Patients can access the support of a dietitian through HealthLink BC.

Appendix F: Therapeutic Phlebotomy Using an 18 Gauge Cannula

The standard equipment provided for phlebotomy is a blood collection unit with a 15 gauge stainless steel needle attached to the unit. The large inflexible needle makes venipuncture difficult if the patient has poor or limited venous access.

The equipment and procedure used here are effective and yet:

- provide more choice of venous access
- patients report the procedure is more comfortable as the cannula is smaller and softer
- patients and nurses report less bleeding post cannula removal.

Equipment

1. 18 ga x 11/4 inch teflon coated IV catheter
2. extension set, luer lock adapters, 38 cm
3. injection cap, 7/8 inch, male luer lock
4. single blood pack unit without anticoagulant
5. BP cuff
6. alcohol swabs
7. sterile 2 x 2 inch gauze
8. tape
9. clamps x 2
10. weigh scale
11. stretcher with adjustable height
12. clean gloves

Procedure

A. Prepare patient

1. provide explanation
2. lay patient down
3. baseline BP and pulse
4. apply heat to arms prn
5. provide a handgrip prn
6. sedation as ordered

B. Prepare equipment

1. open extension set, close clamp
2. attach injection cap to female end of extension unit
3. clean injection cap with alcohol swab
4. insert needle of blood collection unit into injection cap

C. Perform venipuncture

1. BP cuff to 90 mm Hg, clamp to prevent leakage
2. select and clean site
3. glove
4. perform venipuncture, advance cannula to hub
5. attach male adapter to IV device
6. release pressure
7. secure cannula: tape extension set to arm; gauze over venipuncture site

D. Perform phlebotomy

1. open clamp on extension set
2. apply pressure by pumping BP cuff to 60 mm Hg
3. lower collection unit to scale to measure volume
4. adjust flow by the height of bed and pressure of cuff
5. on completion, release BP cuff, clamp extension set, and remove IV device
6. apply pressure, dress site
7. monitor patient and discharge per protocol