GEC•KO Point of Care
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Red Flags to identify patients at risk of **Hereditary Hemochromatosis** most likely to benefit from genetic testing and/or referral to genetics

Personal History HH Red Flags	Family History HH Red Flags
• Biochemical evidence of iron overload (>45% fasting transferrin saturation (TS) and >300µg/L serum ferritin (SF) in men and post-menopausal women or >200µg/L SF in pre-menopausal women.) Biochemical evidence of iron overload will be present before the onset of symptoms. • Unexplained chronic liver disease and increased transferrin saturation ***Elevation of ferritin alone is not necessarily due to iron overload. Ferritin is an acute phase reactant and can be elevated due to infection, inflammation and malignancy.*** *Individuals with HH occasionally demonstrate a normal TS and an elevated ferritin. If clinical suspicion is high and/or the patient has a family history of HH, genetic testing is still warranted*	• Adults with a first-degree relative (sibling, parent or child) who is a C282Y/C282Y homozygote (2 mutated copies of the gene). • Symptomatic adults with a first-degree relative (sibling, parent or child) with one of the following genetic test results: ○ C282Y/H63D (compound heterozygote - 2 different mutated copies of the gene) ○ C282Y/S65C (compound heterozygote) ○ C282Y heterozygote (carrier - 1 mutated copy of the gene) • Family history suggestive of HH (i.e. iron overload, and/or liver disease, type II diabetes, arthritis, heart disease, particularly when two or more are present in an individual)

HH: Hereditary Hemochromatosis

Genetic testing for HH is performed in a specialized hospital laboratory on a blood sample. Click here to find your closest molecular genetics laboratory and the requisition to order testing. Many laboratories prefer that you attach their requisition to the Provincial Ministry of Health requisition. This process will expedite and simplify genetic testing when blood is drawn at a community laboratory.

Children do not require genetic testing for HH. [For conditions that will not present until adulthood (susceptibility or predictive testing) and where there is no benefit to the child, testing should be deferred until the child is competent to understand the purpose of the test and make an autonomous decision.] General population screening for *HFE*-HH is not recommended as the disease penetrance is low.

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Screening and surveillance recommendations for individuals who have a positive genetic test result for Hereditary Hemochromatosis.

***HFE* mutations identified**	**Risk of iron overload**	**Recommendation**
C282Y/C282Y	Highest risk of developing iron overload (38-50%); nonetheless, many of these individuals never accumulate enough iron to cause disease (about 10-33% will develop HH-related symptoms.	• Annual monitoring of TS and SF • Elevated: >45% TS and >300µg/L SF in men and post-menopausal women, or >200µg/L SF in pre-menopausal women • If elevated, consider referral to specialist (gastroenterologist/ hematologist) to be assessed for complications and consideration of treatment
C282Y/H63D	About a 2% lifetime risk of developing iron overload	
C282Y/S65C	Low lifetime risk of developing iron overload - similar to C282Y/H63D	
H63D/H63D	About a 1% lifetime risk of developing iron overload	

HH: Hereditary Hemochromatosis

Treatment is usually initiated and monitored by a specialist (e.g. haematologist or gastroenterologist). Therapeutic phlebotomy, which is safe and effective, is the mainstay of treatment for iron overload. Phlebotomy treatment for HH is recommended when there is convincing evidence of iron overload on iron indices demonstrated over time in a patient who is symptomatic, has evidence of end-organ damage and/or has a family member with iron overload due to HH. Treatment in other circumstances may also be appropriate.

With early identification of at-risk individuals, appropriate surveillance of iron indices, and treatment when necessary, many complications can be avoided.

For more information on Hereditary Hemochromatosis see the complete GEC-KO Messenger at www.geneticseducation.ca

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