# MEMORANDUM

TO: All physicians

FROM: Dr. Debra Bergstrom, Hematology Laboratory Utilization Committee Chair
Division of Hematology/Division of Hematopathology

DATE: December 20, 2017

SUBJECT: **Hereditary Hemochromatosis Testing**

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The Hematology Laboratory Utilization Committee (HLUC) was formed in 2013 to promote the effective and appropriate utilization of laboratory resources.

In early 2016, the laboratory implemented restricted processing of heritable thrombophilia tests to requests from physicians with expertise in the diagnosis and management of thrombosis. This was done to ensure that these tests were being done for recognized indications, after appropriate counselling, in target patient populations.

We are now undertaking a project to similarly restrict genetic testing for hereditary hemochromatosis to patients who meet the appropriate criteria. Hereditary hemochromatosis is an inherited disorder of iron metabolism that is most commonly due to a mutation in the HFE gene. Homozygotes for the HFE C282Y mutation are highly likely to develop clinical iron overload. About 15% of those carrying one copy of the C282Y mutation and one of the H63D (compound heterozygotes) develop clinical disease, often in the setting of another risk factor such as alcohol use, while the other 85% have elevated iron levels but do not necessarily develop clinical disease. Homozygosity for H63D is rarely associated with clinical disease, and carrier status for either mutation is not associated with clinical disease. Other rare, non-HFE mutations exist but are not part of our routine hemochromatosis testing.

Initial screening usually consists of a ferritin level and iron studies (serum iron, total iron binding capacity and transferrin saturation). An elevated serum ferritin in isolation is non-specific and can be seen in many reactive and inflammatory states. Iron studies should therefore be performed before a diagnosis of iron overload is considered. The Canadian Hemochromatosis society recommends genetic testing for hemochromatosis if the transferrin saturation is greater than 45%[1]. If the transferrin saturation is normal or low, alternative causes of hyperferritinemia (such as chronic alcohol consumption, underlying inflammatory state, metabolic syndrome, neoplasm, or non-alcoholic fatty liver disease), should be ruled out before considering genetic testing. If genetic testing is indicated, as with all testing for heritable conditions, appropriate genetic counselling should be provided before and after testing is performed[2]. The 2011 Practice Guideline for the Diagnosis and Management of Hemochromatosis by the American Association for the Study of Liver Diseases (AASLD) provides comprehensive recommendations to guide testing[3].

Current guidelines do not recommend HFE-HH testing of minors as HFE-HH does not present until adulthood; HFE-HH testing should be deferred until such time as an individual is able to receive appropriate counselling and decide whether they wish to proceed with testing[4].

Once restricted testing is put in place, genetic testing for HFE hereditary hemochromatosis (C283Y and H63D HFE mutations) will be performed in adult patients who have elevated iron studies including a transferrin saturation >45%. **Genetic testing will not be performed in isolated hyperferritinemia in the absence of**

**transferrin testing or if the transferrin saturation is normal. Results of transferrin saturation levels must be provided with the requisition for testing to proceed.**

Restrictions are proposed to take effect by the end of January 2018. If you have any feedback or questions, please contact me by email at debra.bergstrom@easternhealth.ca or fax at (709) 777-8374 before we move ahead with this initiative.

Sincerely,

Debra Bergstrom, MD, FRCP(C)
Division of Hematology/Division of Hematopathology, Eastern Health

References:

[1] Canadian Hemochromatosis Society, "Diagnosis and Testing," 2013. [Online]. Available: https://www.toomuchiron.ca/hemochromatosis/diagnosis-testing/. [Accessed: 18-Oct-2017].

[2] R. E. Ensenauer, V. V Michels, and S. S. Reinke, "Genetic testing: practical, ethical, and counseling considerations.," *Mayo Clin. Proc.*, vol. 80, no. January, pp. 63–73, Jan. 2005.

[3] B. R. Bacon, P. C. Adams, K. V Kowdley, L. W. Powell, and A. S. Tavill, "Diagnosis and management of hemochromatosis: 2011 Practice Guideline by the American Association for the Study of Liver Diseases," *Hepatology*, vol. 54, no. 1, pp. 328–343, 2011.

[4] Canadian Paediatric Society, "Guidelines for genetic testing of healthy children," *Paediatr Child Heal.*, vol. 8, no. 1, pp. 42–45, Jan. 2003.