Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate a discussion between a provider and their patient.

Genetic Insights test results: **Hereditary hemochromatosis**

Key results

A DNA variant associated with hereditary hemochromatosis, known as c.845G>A (p.Cys282Tyr), was found in both copies of the *HFE* gene.

Next steps

Clinical recommendations	Resources
Genetic Insights is a genetic screening test and not intended for diagnosis. *Iron studies including serum transferrin saturation and ferritin are recommended for clinical correlation of this result.*	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Quest Diagnostics® offers iron studies that can be ordered through your EHR or from the Quest online Test Directory: testdirectory.questdiagnostics.com/test/home **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Consider a referral to a hereditary hemochromatosis specialist, such as a gastroenterologist, for further clinical management.	The American Liver Foundation offers tools to search for a specialist: liverfoundation.org/for-patients/resources/locate-a-specialist/
Consider referring your patient to a genetic counselor. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights dashboard at no additional cost. To find a genetic counselor practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. Your results are linked to a condition called hereditary hemochromatosis. As a next step, we can order an iron test to check your iron levels. People with hereditary hemochromatosis can have increased iron in their blood, although most people never have increased iron or related symptoms.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is hereditary hemochromatosis?

HFE-associated hemochromatosis (also known as hereditary hemochromatosis) is an inherited condition characterized by increased absorption of dietary iron which, if untreated, may lead to iron overload disorder.[4]

If left untreated, hereditary hemochromatosis can lead to organ damage, including liver cirrhosis.[3,4]

About 24% of males and 14% of females with the 2 *HFE* DNA variants that this genetic test detected will develop symptoms or complications of iron overload.[5]

Symptoms of iron overload typically appear between age 40 to 60 years in males and post-menopause in females. Symptoms may include weakness, fatigue, and weight loss. Others include abdominal pain, arthritis, diabetes, heart failure or arrhythmia.[3,4]

Clinical diagnosis and treatment are based on abnormal iron studies.[2,4]

The most common type of hemochromatosis is the result of 2 DNA variants, 1 in each copy of the *HFE* gene.[3,4]

People with a single DNA variant are considered carriers and do not have hereditary hemochromatosis.

See the Management options section for more detail.

Patient conversation starters:

Hereditary hemochromatosis is a genetic condition that can cause too much iron in the blood and body. If not treated, the iron can build up over time and can lead to damage in certain organs.

There is treatment available for people with too much iron in the blood. However, most people with this condition don't ever develop signs or symptoms or have any related health problems.

What this result means for family members

HFE-associated hemochromatosis is an autosomal recessive condition. Family members may have the same DNA variant(s).

Biological parents of an individual with 2 DNA variants are likely carriers of hereditary hemochromatosis.[4]

Full siblings have a 1 in 4 chance of also having hereditary hemochromatosis and a 1 in 2 chance of being carriers.

The status of children of people with hereditary hemochromatosis depends on the genetics of the other biological parent. Children are at least carriers and may have hereditary hemochromatosis only if the other parent is also a carrier.

In people with confirmed *HFE*-associated hemochromatosis, cascade genetic testing and/or iron studies for family members age 18 years or older may help inform their risk for iron-overload.

A genetic counselor can help determine the most appropriate testing options. Therefore, it is recommended that people share their results with their biological relatives.

Patient conversation starters:

Hereditary hemochromatosis runs in families.

Since you have 2 DNA variants linked to hereditary hemochromatosis, each of your biological parents most likely passed one of them to you. This means that both of your parents are either carriers or may have the condition.

This also means that your brothers and sisters have a higher chance of having hemochromatosis or being a carrier of it.

Each of your biological children will likely be a carrier of hereditary hemochromatosis. They also have a higher chance of having the condition if their other parent has any DNA variants linked to hereditary hemochromatosis.

Sharing your results with your family members may be helpful so they can discuss hereditary hemochromatosis with their healthcare providers.

Management options

There are options for prevention, monitoring, and treatment for people with *HFE*-associated hemochromatosis. Clinical guidelines from the American Association for the Study of Liver Disease[2] include:

Purpose	Management details
Iron overload detection	For people with *HFE*-associated hemochromatosis, a combination of fasting transferrin saturation and serum ferritin should be obtained If iron levels are normal, yearly follow-up iron evaluation should be performed
Iron overload treatment	In those with *HFE*-associated hemochromatosis and iron overload, therapeutic phlebotomy is recommended weekly. Target levels should be a ferritin level of 50 ug/L-100 ug/L
Iron overload and complication prevention	Vitamin C and iron supplements and high alcohol consumption should be avoided
Family member testing	In people with iron-overload and *HFE* variants, screening (iron studies and *HFE* variant analysis) of first-degree relatives to detect early disease and prevent complications is recommended For children, *HFE* testing in the other parent, if possible, is recommended to be performed first because if those results are negative, the child is not at risk and no further testing is required. The American Medical Association does not recommend genetic testing for people under the age of 18 unless it would affect their medical care during childhood[1]

Patient conversation starters:

There are treatment options for people with hereditary hemochromatosis. Treatment is based on the iron levels in the blood. If there is too much iron, people can get regular blood draws to help remove extra iron. Talking with a specialist in hereditary hemochromatosis to help with treatment options is also important.

See current guidelines for complete recommendations. Recommendations may change over time.
If the test result is confirmed, local centers of excellence should be consulted for further clinical management. Consider a referral to a hereditary hemochromatosis specialist, such as a gastroenterologist, for further clinical management.

Additional resources

The following advocacy groups have additional information and resources about hereditary hemochromatosis:

American Liver Foundation: LiverFoundation.org
Iron Disorders Institute, Hemochromatosis.org: Hemochromatosis.org

References

1. American Medical Association. Code of Medical Ethics Opinion 2.2.5: Genetic Testing of Children. Updated November 14, 2016. Accessed June 2, 2022. https://www.ama-assn.org/delivering-care/ethics/genetic-testing-children
2. Adams P, Altes A, Brissot P, et al. Therapeutic recommendations in HFE hemochromatosis for p.Cys282Tyr (C282Y/C282Y) homozygous genotype. *Hepatol* Int. 2018;12(2):83–86. doi:10.1007/s12072-018-9855-0
3. Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS. Diagnosis and Management of Hemochromatosis: 2011 Practice Guideline by the American Association for the Study of Liver Diseases. *Hepatology*. 2011;54(1):328–343. doi:10.1002/hep.24330
4. Barton JC, Edwards CQ. HFE Hemochromatosis. April 3, 2000. Updated December 6, 2018. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2022. https://www.ncbi.nlm.nih.gov/books/NBK1440/
5. Gallego CJ, Burt A, Sundaresan AS, et al. Penetrance of hemochromatosis in HFE genotypes resulting in p.Cys282Tyr and p.[Cys282Tyr];[His63Asp] in the eMERGE Network. *Am J Hum Genet*. 2015;97(4):512-520. doi:10.1016/j.ajhg.2015.08.008

This information is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by a healthcare provider.

Individuals should talk with a healthcare provider about the meaning of genetic test results and before stopping, starting, or changing any medication or treatment.

Genetic Insights is a test developed and performed by Quest Diagnostics. The test results are not diagnostic and do not determine overall chances of developing a disease or health condition. The tests are not cleared or approved by the US Food and Drug Administration.

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