Sonic Genetics
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Genetic testing in familial hypercholesterolaemia

Bulletin for Doctors | May 2020

This bulletin describes the care pathway for familial hypercholesterolaemia that is provided through local Sonic Healthcare pathology practices across Australia.

Familial hypercholesterolaemia (FH) is an autosomal dominant disorder, in which the liver's ability to remove LDL-cholesterol from the blood is impaired. It causes elevated LDL-cholesterol and premature atherosclerotic cardiovascular disease (CVD). FH is the most common inherited cause of premature CVD and affects ~100,000 people in Australia. Early detection and initiation of lifestyle and lipid-lowering treatment of people with FH has been shown to reduce CVD. Currently, 90% of patients with FH have not been diagnosed and represent a missed opportunity to reduce the prevalence of CVD.

A clinical diagnosis of FH can be made on the basis of LDL-cholesterol levels, personal and family history and clinical features, including corneal arcus and tendon xanthomata.[1] While a clinical diagnosis of FH is useful in differentiating it from multifactorial hypercholesterolaemia, the partial treatment of hypercholesterolaemia often masks these features. For this reason, clinical and biochemical features alone are often not sufficient to make a firm diagnosis of FH.

Genetic testing in patients with FH

A pathogenic variant in *LDLR*, *APOB* or *PCSK9* gene causes autosomal dominant FH.

Genetic testing of patients with FH is important for a number of reasons:

- Genetic confirmation is the gold standard for diagnosing FH.
- Patients with genetically confirmed FH have a higher CVD risk than non-FH patients for any given LDL-cholesterol level. They warrant aggressive therapy and monitoring.
- Patients with genetically confirmed FH may be able to access evolocumab (PCSK9-inhibitor) on the PBS, depending on their LDL-cholesterol level and presence of CVD.
- Relatives of a patient with a pathogenic variant are at 25–50% risk of inheriting the variant. Family testing for the variant is rebated by Medicare, and allows accurate early detection and treatment.
- Medication compliance is increased among patients with genetically confirmed FH.

Medicare-rebated testing from May 2020

Genetic analysis will be rebated by Medicare, provided the patient has:

- a Dutch Lipid Clinic Network score of at least 6; *or*
- an LDL-cholesterol concentration of 6.5 mmol/L or more in the absence of secondary causes; *or*
- an LDL-cholesterol of 5.0 mmol/L or more with signs of premature/accelerated atherogenesis.

Requests for rebated testing of the three genes must be made by a specialist. If a pathogenic variant has already been identified in the family, the patient should be tested for that variant (cascade testing), rather than have the three genes examined. Comprehensive testing of these genes is also available for a private fee ($1,200* includes genetic counselling) for patients who may not meet Medicare criteria.

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Once a pathogenic variant has been identified, cascade testing of first- and (as appropriate) second-degree relatives can be ordered by any medical practitioner. Cascade testing is preferably performed by the age of 10 years, as treatment initiated during childhood is effective in reducing the long-term risk of CVD.

Testing and genetic counselling through your local Sonic Healthcare pathology practice

Sonic Genetics provides comprehensive genetic testing for FH, using next generation sequencing in our accredited laboratory in Sydney, including deletion analysis of the LDLR gene. Our panel also includes testing of a fourth gene, *LDLRAP1*, which causes autosomal recessive hypercholesterolaemia.

Sonic Genetics also provides pre- and post-test genetic counselling, via phone and at no additional cost to the patient. Pre-test genetic counselling may be provided by the requesting specialist or a genetic counsellor. Consent for testing must be documented in writing using the Sonic Genetics Consent Form or an equivalent. Our genetic counsellors can also assist cascade testing by notifying family members of the availability of rebated testing for the family's variant.

Requests for testing for FH are preferably made on our dedicated request form, available from www.sonicgenetics.com.au/fh, as this includes additional information for patients. Please indicate which of the Medicare criteria apply for rebated testing. If you request genetic counselling, or if written consent is not provided with the request form, we will contact the patient to arrange pre-test genetic counselling and provision of consent by phone, usually within 48 hours. Patients who decline to proceed with testing will not be liable for any fee.

Results will usually be available within 4–6 weeks of receipt of the sample by the genetics laboratory in Sydney. Two tubes of EDTA blood are required for testing.

National Sonic Genetics' FH program

FH is a common disorder, involving multidisciplinary care provided by general practitioners, lipid specialists, cardiologists and two disciplines of pathology (chemistry and genetics). Sonic Genetics has developed a national program for the triage and testing of patients with FH. We are committed to developing educational resources about FH for doctors and patients.

The chemical pathologists at the local Sonic Healthcare pathology practice supervise lipid reporting. Our FH testing program is supervised by Dr Melanie Galea (Genetic Pathologist) and Assoc. Professor Damon Bell (Chemical Pathologist/Endocrinologist). These experts in FH are available to assist you.

Further details are available from the Sonic Genetics website, www.sonicgenetics.com.au/fh or contact Sonic Genetics on 1800 010 447 or info@sonicgenetics.com.au for further information.

Reference

1. Dutch Lipid Clinical Network Score (DLCNS) Online Calculator [Internet]. FH Australasia Network, 2020. [Accessed April 2020]. <www.athero.org.au/fh/calculator>

* Correct at time of printing