Ordering Guidance for Genetic Testing for Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is an inherited disorder of lipid metabolism that results in elevated levels of low-density lipoprotein (LDL) cholesterol, and risk of heart disease at an early age. FH affects 1 in 250-300 Canadians; however, most are undiagnosed. Early identification of FH supports the use of medication to normalize life expectancy and genetic testing of at-risk relatives. Please see Familial Hypercholesterolemia Implementation Recommendations for additional details.

Individuals meeting one or more of the following criteria should be offered FH genetic testing:

1. **Family history of confirmed FH**: Disease-causing pathogenic/likely pathogenic variant (mutation) in a close (1st or 2nd degree) blood relative (e.g. sibling, child, parent, parents' sibling, grandparent)
2. **Extremely high LDL:** Personal history of high LDL cholesterol level of ≥ 8.5 mmol/L at any age
3. **High LDL with additional features:** Personal history of untreated elevated LDL cholesterol level (not due to secondary causes). If baseline/untreated LDL cholesterol is unknown, an imputed level can be derived using the CardioRiskCalculator:
   - Untreated LDL cholesterol level ≥ 5.0 mmol/L for age 40 years and over
   - Untreated LDL cholesterol level ≥ 4.5 mmol/L for age between 18 years and 39 years
   - Untreated LDL cholesterol level ≥ 3.5 mmol/L for age under 18 years

   AND at least one of the following:
   - Tendon xanthomas and/or corneal arcus in the patient
   - First-degree relative with high LDL cholesterol level (not due to secondary causes)
   - Proband or first-degree relative with early onset atherosclerotic cardiovascular disease (men under 55 years; women under 65 years)
   - Limited family history information (e.g., adopted)
4. **Clinical judgement**: A clinician may use clinical judgement to order genetic testing in individuals who do not fit the above if advised by genetics and/or lipid disorder expert(s).

Additional considerations for the eligibility criteria above:

- Genetic testing in the pediatric population can be offered at any age, ideally in the first decade of life, guided by family history and/or lipid screening results.
- Prenatal diagnosis for FH does not change medical management.
- Routine results are expected in 6 to 8 weeks; expedited testing is not required.

How do I order FH genetic testing for my patient?

Please complete an FH genetic testing requisition from one of the testing labs: Hamilton Regional Laboratory Medicine Program, London Health Sciences Centre, and Trillium Health Partners – Credit Valley Site. Your patient can take the requisition to a local community laboratory for bloodwork.

What should I do with abnormal or uncertain results?

For guidelines on management of FH, please see the Canadian Cardiovascular Society position statement. Certain results (e.g., findings beyond your comfort level, variant of uncertain significance (VUS)) may require consultation with genetics and/or genetic counselling for your patient. Please consider the following options as needed:

- Visit OTNhub to connect with a genetics specialist through OTN eConsult
- Visit Ontario Health to find your local genetics clinic.

Need this information in an accessible format? 1-877-280-8538, TTY 1-800-855-0511, info@ontariohealth.ca.
Document disponible en français en contactant info@ontariohealth.ca