Familial Hypercholesterolaemia

Disclaimer

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Background – About Familial Hypercholesterolaemia (FH)

- FH is a common autosomal dominant-inherited disorder present from birth and occurs in 1 in 250 people. It is associated with elevated plasma low-density lipoprotein cholesterol (LDL-c), and premature coronary heart disease.
- Children of affected individuals have a 50% chance of inheriting the condition.
- If untreated, there is a high incidence of premature cardiovascular disease:
  - 50% by age 50 years in males
  - 30% by age 60 years in females
- Early diagnosis and life-long treatment reduces the risk of premature coronary heart disease (CHD).

Assessment

1. Use the Dutch Lipid Clinic Network Score (DLCNS) to clinically diagnose FH by accessing the DLCNS online calculator or DLCNS printable form.

   **Dutch Lipid Clinic Network Score (DLCNS)**
   
   The diagnosis is based on the total score:
   - Definite FH > 8
   - Probable FH 6 to 8
   - Possible FH 3 to 5
   - Unlikely FH < 3

   Cardiovascular risk calculators are not appropriate for patients with suspected or confirmed FH, as they are already at high risk.

2. Exclude secondary causes of hypercholesterolaemia.

   **Secondary causes of hypercholesterolaemia**
   - Hypothyroidism
   - Nephrotic syndrome and chronic kidney disease (CKD)
   - Cholestatic biliary disease
   - Diabetes
   - Anorexia nervosa
   - Hypopituitarism
   - Medications – thiazide diuretics, corticosteroids, oral contraceptives, cyclosporin, atypical antipsychotics, anticonvulsants

3. Consider referral for genetic testing for FH in consultation with the specialist.

   **Genetic testing for FH**
   - Genetic testing for FH is not essential for diagnosis or management, but may be beneficial in:
     - clarifying the diagnosis.
     - investigating a specific family mutation.
     - determining the level of risk to the patient, where a severe pathogenic mutation is identified.
     - determining suitability for PBS subsidised treatment with Evolucamab (lipid lowering human monoclonal antibody) if DLCNS score is ≤ 6.
• If DLCNS is ≥ 7, genetic testing is not required for PBS medication subsidy.
• Approximately 20% of cases of FH with a definite clinical diagnosis will not have a mutation.

4. If the patient has a high CVD risk or strong family history of premature atherothrombotic disease, consider plasma **lipoprotein(a) (Lp(a))**. Although not recommended for routine screening, it is an important, independent predictor of cardiovascular disease.

**Lipoprotein(a) (Lp(a))**
Lp(a) is an independent predictor of cardiovascular disease.
It is not recommended for routine screening (not Medicare rebatable).
Indications for screening:
• Premature cardiovascular disease
• Early onset aortic sclerosis
• Familial hypercholesterolaemia
• Family history of:
  • premature cardiovascular disease
  • elevated lipoprotein(a)
  • aortic sclerosis
• Recurrent cardiovascular disease despite statin treatment
• Persistent elevated LDL despite statin treatment

If results indicate elevated levels, seek advice from a lipid disorders specialist.

**Lipoprotein(a) results**
Lp(a) is reported in several different ways, as mass (mg/dL, grams/L, or mg/L) or as particle numbers (nmol/L):
- Normal level: Lp(a) < 30 mg/dL (< 75 nmol/L or 0.3 grams/L)
- Lp(a) > 30 mg/dL (> 75 nmol/L or 0.75 grams/L) are associated with a 2 to 3-fold increased risk of cardiovascular events independent of conventional risk markers.
- Lp(a) > 50 mg/dL (> 125 nmol/L) are associated with a markedly increased risk.

In terms of risk:
- Desirable: < 14 mg/dL (< 35 nmol/L)
- Borderline risk: 14 to 30 mg/dL (35 to 75 nmol/L)
- Moderately high risk: 31 to 50 mg/dL (75 to 125 nmol/L)
- Very high risk: > 50 mg/dL (> 125 nmol/L)

Management

1. Consider referral to a lipid disorders specialist if:
   • patient has a DLCNS > 5.
   • difficult to control low-density lipoproteins (LDL) > 3.3 mmol/L in patients with coronary heart disease and with familial hypercholesterolaemia.

2. For lipid management, follow the Hyperlipidaemia pathway. If no contraindications commence a statin. See PBS Criteria for Familial Hypercholesterolaemia.

3. Encourage lifestyle modification:
   • diet
• **smoking cessation**
• exercise
• alcohol.

4. Offer cascade screening of first-degree relatives (parents, siblings, and children), with consent of the patient, via plasma LDL-c testing.

5. If starting a statin in a female patient of childbearing age, give **contraception advice** and **pre-pregnancy counselling**.

   - **Contraception advice**
     - Statins are contraindicated in pregnancy, so effective contraception is essential.
     - Long-acting reversible contraceptives (LARCs) are particularly useful.
     - Combined oral contraceptives can increase TG levels. Risk may exceed benefit for some women with hyperlipidaemia, especially if they have multiple cardiovascular risk factors.

   - **Pre-pregnancy counselling**
     - Discontinue statins and other systemically absorbed lipid regulating drugs 3 months prior to conception, and during pregnancy and lactation.
     - Bile acid sequestrants are the only safe agents to control hypercholesterolaemia in pregnancy and lactation – colesevelam is more tolerable than older resins.

     **Review at least annually.**

6. If patient is pregnant with heterozygous FH, consider referral to a lipid disorders specialist for lipoprotein apheresis.

### Referral

- Consider referral to a lipid disorders specialist if:
  - patient has a DLCNS > 5.
  - difficult to control low-density lipoproteins (LDL) > 3.3 mmol/L in patients with coronary heart disease and with familial hypercholesterolaemia.
- If required, the specialist may refer for genetic testing.

### Information

#### For health professionals

**Further information**

- Australian Family Physician – [Detecting Familial Hypercholesterolaemia in General Practice](#)
- FH Australasia Network:
  - Dutch Lipid Clinical Network Score (DLCNS) Online Calculator
  - FH and Lp(a) Specialists
- The University of Notre Dame Australia – [Familial Hypercholesterolaemia: Challenges in Primary Care](#)
For patients

- FH Australasia Network:
  - Familial Hypercholesterolaemia Clinical Support Service
  - What You Need to Know: Familial Hypercholesterolaemia (FH)
- NPS Medicinewise – High Cholesterol: Get the Lowdown

References


Select bibliography


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