key points

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Familial hypercholesterolaemia (FH) is a relatively common genetic disorder, the heterozygous form affecting 1 in 500 people in the UK. It is caused by mutations in the hepatic proteins involved in the clearance of LDL-C from the circulation. The homozygous form is very rare and in practice almost all patients seen will have the heterozygous form.

FH accounts for around 10% of all hyperlipidaemias. It is a risk factor for the development of premature atherogenesis, and therefore coronary heart disease.

In the heterozygous form of the condition typical TC levels are 7-13 mmol/l (>13mmol/l in the homozygous form). HDL-C levels are typically average or reduced, while triglyceride levels are usually within the normal range (< 1.7 mmol/l). The clinical corollary of this is the development of CHD at an early age if untreated; this is typically in the fourth decade in men who are heterozygous and a decade later in women.

The diagnosis of FH rests on the Simon Broome criteria, essentially, it requires elevation of LDL-C, plus clinical evidence of hypercholesterolaemia such as tendon xanthomata, and evidence of a family history. Patients with definite or possible FH need to undergo further testing which usually requires referral to a lipid clinic.

The initial finding of hypercholesterolaemia does not differentiate FH from other dyslipidaemias. Further investigations are therefore required to narrow the diagnostic field. In addition to the lipid profile (TC, HDL-C, LDL-C and triglycerides), baseline investigations should include: urea, creatinine and electrolytes, estimated glomerular filtration rate, liver function tests, fasting blood glucose, thyroid function tests, full blood count, urinalysis for blood, protein and glucose.

The key points in the history are to ascertain the family history of (usually premature) cardiovascular disease, and to check for the presence of additional risk factors. It is quite possible that some patients with FH will have symptomatic cardiovascular disease at first presentation, so enquiries should be made about suggestive symptoms such as angina and intermittent claudication.

All first-degree relatives, not just the children, of FH patients have a 50% risk of having the condition; and should be traced and tested.

NICE recommends high-intensity statin therapy as the first line of treatment. Statins are of proven efficacy in FH and have a good safety record, although myopathy or even more rarely, rhabdomyolysis may occur. The recommended target is a reduction in initial LDL-C by 50%. Most children with FH will require drug treatment by their midteens, if not earlier.