DR. JEFF C.H. DONOVAN

DERMATOLOGIST, SPECIALIZING IN HAIR LOSS

4370 Lorimer Road
Suite 334B
Whistler, BC, Canada
V8E 1A6

Tel: 604.283.1887
Fax: 604.648.9003
Email: office@donovanmedical.com
Web: www.donovanmedical.com

FAMILIAL HYPERCHOLESTEROLEMIA

What is Familial (heterozygous) hypercholesterolemia ?

Familial hypercholesterolemia ("FH" for short) affects about 1 in every 250 people worldwide. About 150,000 Canadians have this condition and most simply never get diagnosed. In fact, it is estimated that only about 10 % of patients with FH ever get diagnosed. For patients who are ultimately proven to have FH the risk of cardiovascular disease is about 20 times above the general population.

This condition itself does not cause hair loss but has very important health implications as patients may experience an early onset cardiovascular disease.

What are the genes affected in FH?

The condition is transmitted from mother or father and cause elevation in LDL. Usually the triglycerides are either normal or only a slight bit elevated.

The inherited genes often affect LDL, APOE or PCSK9. Other genes may also be involved.

Why is it important to diagnose FH?

Individuals are at risk for early heart disease, including heart attacks. Individuals with mutations in one of the genes mentioned above have an up to 20 fold increased risk of heart disease. If the individual is a smoker, has high blood pressure, is obese, the risk is increased even further.

Even if FH is not confirmed, individuals who have an elevated LDL have an increased risk of heart disease as well and will benefit from treatment.

Can treatment benefit the long term outcome?

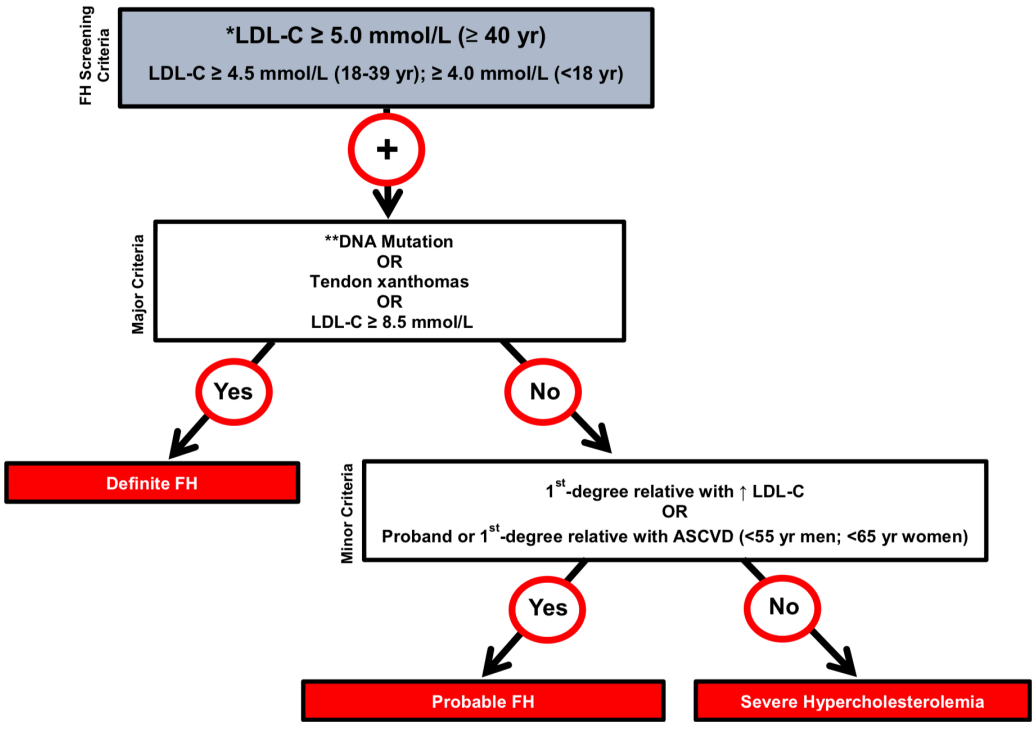
Yes, treatment can reduce the chances of developing heart disease in patients with FH and in those with elevated LDL who don't have FH. Treatment focuses on several aspects including:

a) *Smoking cessation*
b) *Improving physical activity*
c) *Lowering blood pressure if the patient has high blood pressure*
d) *Improving diet*
e) *Limiting or treating diabetes*
f) *Use of medications such as statins, ezetimibe and other treatments*

Current guidelines suggest that an LDL less than 3.5 mmol/L is a reasonable goal and some suggest that aiming for less than 2.5 mmol/L is a better goal. If there is any evidence of heart disease already, the goal should be to aim for an LDL less than 2.0 mmol/L.

CANADIAN GUIDELINES FOR DIAGNOSING FAMILIAL HYPERCHOLESTEROLEMIA

FROM: Brunham et al. Canadian Cardiovascular Society Position Statement on Familial Hypercholesterolemia: Update 2018. Canadian Journal of Cardiology. 34(12); 1553-1563



ASCVD includes a) coronary heart disease (CHD), such as myocardial infarction, angina, and coronary artery stenosis > 50%. b) cerebrovascular disease, such as transient ischemic attack, ischemic stroke, and carotid artery stenosis > 50%. c) peripheral artery disease, such as claudication. d) aortic atherosclerotic disease, such as abdominal aortic aneurysm and descending thoracic aneurysm.

TABLE 3. Dutch Lipid Clinic Network Clinical Criteria for Diagnosing Heterozygous FH[a-c]

Criteria		Points[d]
Family history		
A first-degree relative (parent, offspring, or sibling of the patient) aged 18-55 y, women 18-60 y with		
coronary or vascular disease *or*		1
LDL-C level >95th percentile for age and sex		1
Children aged <18 y with LDL-C level >95th percentile for age and sex *or*		2
A first-degree relative with tendon xanthomas or arcus cornealis		2
Personal history of premature ASCVD		
Coronary heart disease		2
Cerebral or peripheral vascular disease		1
Physical examination		
Tendon xanthomas		6
Arcus cornealis at age <45 y		4
Plasma levels of LDL-C (mg/dL)		
>325	**> 8.405 mmol/L**	8
251-325	**> 6.5 mmol/L**	5
191-250	**> 4.9 mmol/L**	3
155-190	**> 4.1 mmol/L**	1
Molecular genetic testing		
Pathogenic variants in *LDLR, APOB, PCSK9*		8

[d]The highest applicable score should be chosen in each diagnostic group. Definite heterozygous FH is considered present if the total score is greater than 8 points, probable FH if the score is 6 to 8 points, and possible FH if the score is 3 to 5 points; if the score is 0 to 2 points, FH is unlikely.

Safarova MS et al. My Approach to the Patient With Familial Hypercholesterolemia. Mayo Clin Proc 2016; 91(6):770

TABLE 4. British Simon Broome Register Criteria[a-d]

	Plasma levels (mg/dL): • Total cholesterol >290 (adult) or >260 (child aged <16 y) or • LDL-C >190 (adult) or >155 (child aged <16 y)	**> 7.5 mmol/L** **> 4.9 mmol/L**
Tendon xanthomas in the patient or any of the patient's first- (parent, offspring, or sibling) or second-degree (grandparent, grandchild, nephew, niece or half-sibling) relatives	Family history of myocardial infarction: • In a first-degree relative before age 60 y • In a second-degree relative before age 50 y	
Molecular genetic testing: pathogenic variant in *LDLR, APOB, PCSK9*	Family history in any first- or second-degree relative of plasma total cholesterol level >290 mg/dL in an adult or >260 mg/dL in a child	
Definite HeFH	**Probable HeFH**	

[a]heFH = heterozygous FH.

[b]SI conversion factor: To convert total cholesterol and LDL-C to mmol/L, multiply by 0.0259.

[c]Clinical criteria adopted in the Japanese population differ mainly in a lower bar for the LDL-C levels and a different cutoff for defining early-onset CHD in women. These criteria for the diagnosis of heFH in patients 15 years and older include (1) pretreatment LDL-C levels of at least 180 mg/dL, (2) tendon xanthomas and/or Achilles tendon thickening (≥9 mm), (3) family history of FH or premature CHD (in males and females <55 and <65 years old, respectively) in first- and second-degree relatives.[60]

[d]A diagnosis of FH is based on a combination of clinical criteria with biochemical results (obligatory), except when there is a positive genetic test.

REFERRALS

Many patients consider referral to St Paul's Hospital for evaluation or to a lipid clinic or to a local endocrinologist or cardiologist who specializes in lipid disorders.

HEALTHY HEART PROGRAM

The prevention Clinic diagnoses and treats disorders related to cholesterol metabolism.

Location and Contact
St. Paul's Hospital
Room 180, 1081 Burrard Street
Vancouver, BC, V6Z 1Y6
Phone: 604-806-8591
Fax: 604-806 8590

REFERENCES

Safarova MS et al. My Approach to the Patient With Familial Hypercholesterolemia. Mayo Clin Proc 2016; 91(6):770

Brunham et al. Canadian Cardiovascular Society Position Statement on Familial Hypercholesterolemia: Update 2018. Canadian Journal of Cardiology. 34(12); 1553-1563