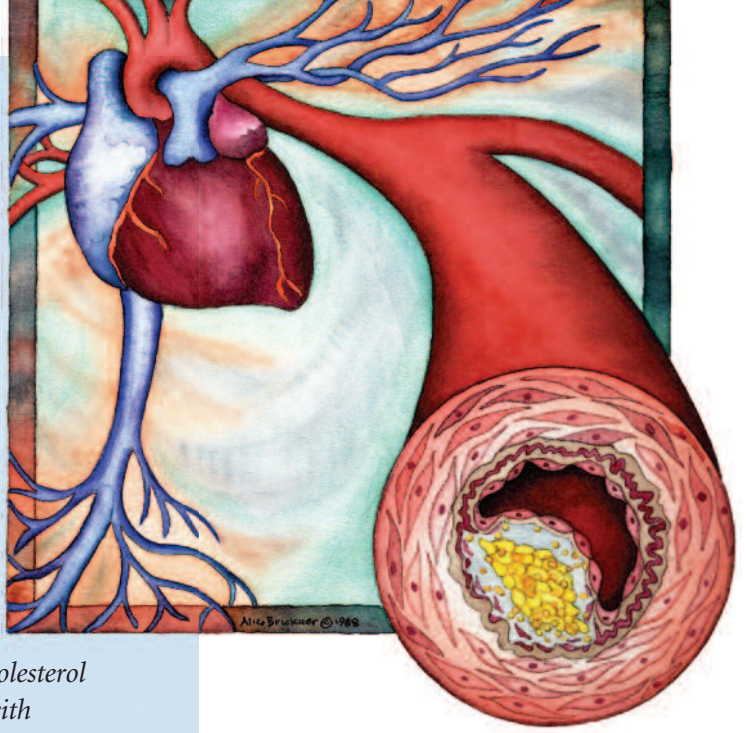
CASE STUDY

Father and daughter with the same cholesterol problem



LEON A. SIMONS MD, FRACP

The initiation of statin therapy in middle-aged people with cholesterol problems is relatively straightforward; however, in teenagers with heterozygous familial hypercholesterolaemia the timing of statin introduction is complex and specialist advice may be required.

Case scenario 1

Mr SB, aged 40 years, was referred in 1998 for specialist review and treatment of a cholesterol problem. He had no symptoms of cardiovascular disease (CVD). At age 14 years, he was found to have a total cholesterol level of 10 mmol/L as part of family testing. His father had died aged 49 years from a myocardial infarction, his cholesterol level being about 14 mmol/L. Mr SB's two younger siblings also had elevated cholesterol levels but with no history of CVD.

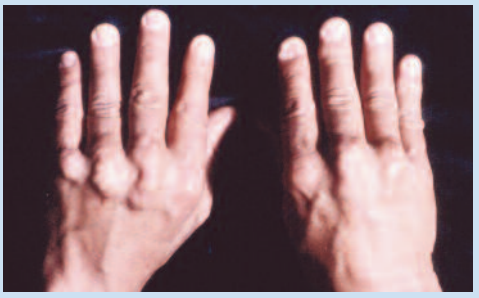
Previous cholesterol therapy for Mr SB was with cholestyramine, but since 1990 he had been taking simvastatin 40 mg/day. He was a nonsmoker and nondrinker. His body mass index was 26.5 kg/m^2 and blood pressure was 120/80 mmHg. He had tendon xanthomas on the dorsum of his hands and in the Achilles tendons bilaterally (see Figure). There were no abnormal cardiovas - cular signs. A resting ECG and a subsequent stress test were within normal limits.

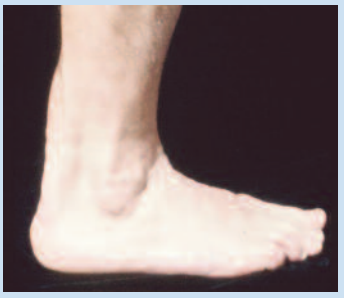
Blood tests (on treatment) showed the following results:

- *total cholesterol level of 7.3 mmol/L (desirable <4.0 mmol/L)*
- *triglycerides 1.2 mmol/L (desirable <2.0 mmol/L)*
- *HDL 1.7 mmol/L (desirable >1.0 mmol/L)*
- *LDL 5.0 mmol/L (desirable <2.0 mmol/L).*

Electrolyte, creatinine, glucose and liver and muscle enzyme levels, thyroid function and full blood count were all within normal limits. A clinical diagnosis of heterozygous familial hypercholesterolaemia (HFH) was made. This syndrome is generally due to an autosomal dominant gene and was discussed in Cardiology Today *in the November 2012 issue.*[1]

Revision of Mr SB's drug therapy was considered necessary and he was switched from simvastatin to atorvastatin 40 mg/day. Eight weeks later his total cholesterol level





Figures 1a and b. Tendon xanthomas in Mr SB who has heterozygous familial hypercholesterolaemia.

Key points

- **Patients with heterozygous familial hypercholesterolaemia (HFH) are at high risk of premature cardiovascular disease, and statin therapy is strongly indicated.**
- **High-dose statin therapy in combination with a second drug such as ezetimibe may be required to achieve goal LDL cholesterol levels in some patients.**
- **The children of patients with HFH should be tested for this condition. Affected patients will need dietary and statin therapy.**
- **The timing of introduction of statin therapy in teenagers is problematical and specialist advice may be required.**

CARDIOLOGY TODAY 2013; 3(2): 33-34

Professor Simons is Associate Professor of Medicine and Director, University of NSW Lipid Research Department, St Vincent's Hospital, Sydney, NSW.

was 6.9 mmol/L and LDL cholesterol level 4.6 mmol/L. Atorvastatin was then increased to 80 mg/day and a further nine weeks later his total cholesterol level was 6.1 mmol/L and LDL cholesterol level 3.8 mmol/L.

Mr SB resided more than 150 km from the specialist's office and he requested, quite reasonably, that further follow up be provided by his GP. Correspondence with his GP about one year later showed that Mr SB was eventually supplemented with ezetimibe and achieved a total cholesterol level of 4.3 mmol/L and LDL cholesterol level of 2.2 mmol/L. He remained free of clinical CVD over the following 13 years.

Case scenario 2

Miss TB, the 16-year-old daughter of Mr SB, was referred for consultant opinion in 2003. Her total cholesterol level at age 5 years was 6.5 mmol/L. Her total cholesterol level was now 7.0 mmol/L, triglyceride level 0.9 mmol/L, HDL level 1.6 mmol/L and LDL level 5.0 mmol/L while following standard dietary advice. Results of all other blood tests, including thyroid function, were within normal limits. Physical examination was unremarkable, and she had neither corneal arcus nor xanthomas. A diagnosis of HFH was made.

Consultant comments

Although statin therapy would seem appropriate for Miss TB, the timing of its introduction is problematical. My personal view is that statin therapy in very young women with HFH can be delayed until they have completed childbearing or until they reach say 25 to 30 years of age, unless there are specific circumstances present that suggest statins should be started earlier. These might include highly premature CVD in a first-degree relative, very high cholesterol readings (e.g. 10 mmol/L or more), the presence of other major coronary risk factors or the patient is anxious and keen to start therapy sooner rather than later. I acknowledge that some experts would be much less conservative in young women with HFH and would introduce statin therapy in the teenage years. My approach is much more aggressive in young men with HFH, given the higher risk of CVD in males.

In the case of Miss TB, there appeared to be no specific circumstances present. At 16 years of age she was keen to continue following dietary advice without drug therapy.

Fast forward to early 2013, almost 10 years later: case 2 continued

Miss TB, now aged 26 years, was referred back to the specialist for a further opinion and treatment in relation to the same issues. Her lipid profile now shows a total cholesterol level of 6.8 mmol/L, triglyceride level 0.8 mmol/L, HDL level 1.4 mmol/L and LDL level 5.1 mmol/L. Results of other blood tests and urinalysis are within normal limits. She is a nonsmoker, in good general health and has been following a careful low saturated fat diet.

Miss TB's LDL cholesterol level is signifi - cantly elevated and the timing of any statin therapy is again discussed. The patient feels that any pregnancy is some years into the future because of her career aspirations. She is now anxious about her risk of premature CVD and it is mutually agreed that she should start statin therapy with rosuvastatin 10 mg daily. She is counselled to suspend statin therapy temporarily if and when a pregnancy was planned (or occurs).

Given the distance Miss TB resides from the specialist's office, follow up by her GP is suggested at intervals of eight weeks to monitor her compliance with the medication and any side effects, to measure lipids, glucose and muscle enzyme levels and to perform liver function tests. Dose uptitration will probably be necessary and, ultimately, she may require a supplementary drug in addition to statin therapy to achieve a goal LDL level of 2.0 mmol/L.

Conclusion

Clinical trials with statin drugs typically run for five years (or less) and have yielded clear evidence of safe and effective CVD prevention. In the real world, patients will use statins for much longer periods of time. Initiation of statin therapy in middle-aged people is straightforward; however, in young patients with HFH the timing of introducing statin therapy is complex and requires careful judgement. **CT**

Reference

1. Simons L. A patient with familial hypercholesterolaemia unable to achieve target LDL-cholesterol levels. Cardiology Today 2012; 2(4): 29-30.

COMPETING INTERESTS: None. The views expressed are purely those of the author.