The slow turnover of sitosterol in these patients is not clearly understood. In normal persons, plant sterols are poorly absorbed and preferentially excreted by the liver. Bhattacharyya first reported\(^1\) a new inherited sterol storage disease.

We report a case of sitosterolemia with premature coronary artery disease which required surgical intervention. A 16-year-old Caucasian girl was referred to us for further investigation after hospitalization elsewhere for chest pain and changes in electrocardiographic precordial leads.

Her family history showed that one uncle had died aged less than 60 from a stroke. At clinical examination no tendon or tuberous xanthomas were found. The electrocardiogram showed an anterior myocardial infarction. A chest X-ray revealed a heart of normal size. Dobutamine echocardiography showed viable tissue in the anteroseptal wall and an ischaemic response in the inferior wall. Thallium 201 showed a scar in the anterior wall. Laboratory examination results were normal including amino acid profile (homocysteine, methionine), vitamin E, A, carotene, lipids, lipoproteins and apolipoproteins. The blood sitosterol was measured by flow cytometry and was found to be 19 mg dl\(^{-1}\).

Coronary arteriography showed occlusion of the left anterior descending and >70% stenosis of the middle right coronary artery, with a 100% occlusion of the posterior descending artery (Fig. 1). At selective angiography both carotid arteries and the abdominal aorta were normal. She had double aortic coronary bypass surgery performed and was discharged with cholestyramine 8 g daily.

In this very rare disease only homozgyous subjects manifest an increase of total plasma sterol concentrations, particularly sitosterol and tendon xanthomias, despite the normal plasma cholesterol concentration. The mechanism for the development of xanthomas and atherosclerosis in these patients is not clearly understood. In normal persons, plant sterols are poorly absorbed and preferentially excreted by the liver. Bhattacharyya et al.\(^1\) suggested that the metabolic defect in sitosterolemia is a combination of enhanced intestinal absorption and a sluggish turnover of sitosterol in the body compared with normal humans. Sitosterol absorption is increased 7- to 16-fold. These altered processes result in a 13 to 17-fold increase of the total sterol and a 22 to 58-fold increase in the sitosterol levels. The slow turnover of sitosterol in these
patients is the result of decreased excretion of sitosterol into the duodenal bile. Salen et al. postulated that decreased hepatic sitosterol excretion into bile helps conserve sterols in the body, while diminished cholesterol synthesis is observed, 26 to 28% lower than that of normals. Nguyen et al. suggested that the reduced cholesterol synthesis is due to a deficiency of 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase. They investigated the activity of HMG-CoA reductase in sitosterolemic patients and controls and found that mononuclear leukocytes from control subjects contained almost twice the total HMG-CoA reductase activity and nearly two to four times the amount of enzyme protein compared to those of sitosterolemic patients.

The function of low density lipoprotein (LDL) receptors is regulated by HMG-CoA reductase so that enzyme activity and LDL receptor function respond in the same way. However, in sitosterolemic homoyzogotes the opposite occurs, with a resulting enhanced LDL receptor function and low HMG-CoA reductase activity. About 76% of plasma sitosterol is carried with LDL, and there is increased uptake of sitosterol carrying LDL via LDL receptors.

The levels of sitosterol in our patient are within the range described in the literature. Normally sitosterol levels do not exceed 0.4 mg dl⁻¹. The behaviour of drugs, such as HMG-CoA reductase inhibitors or bile acid sequestrant resins has not been adequately evaluated in this disease. Nguyen et al. found no influence of lovastatin or a low sterol diet compared to those of sitosterolemic patients and controls. Smitz and his staff for the measurement of blood sitosterol.

G. KOLOVOU
V. VOUDRIS
E. DROGARI
G. PALATIANOS
D. V. COKKINOS
Cardiology and Surgery Department,
Onassis Cardiac Surgery Center.
Athens, Greece

References

Chemotherapy-induced myocardial infarction
Cardiovascular ischaemia has been recognised as a serious, but uncommon complication of treatment with several chemotherapeutic agents. This report describes a young man who developed a myocardial infarction after completion of a chemotherapy regime.

A 30-year-old man with a mixed germ cell tumour was treated for a relapse of his condition with combination chemotherapy. He had no risk factors for ischaemic heart disease. A 10-day course of cisplatin, vincristine and methotrexate was followed by two courses of dactinomycin, cyclophosphamide and etoposide, each over a 5-day period. Three days into each of the latter two courses, he experienced several minutes of indigestion-like chest pain. Three days following completion of the final treatment he developed severe central chest pain associated with vomiting, while walking upstairs. The pain persisted for 10.5 h and had subsided on arrival in the Accident and Emergency Department. An ECG demonstrated ST elevation in the inferolateral leads. Treatment consisted of intravenous nitrates, aspirin and full anti-coagulation with heparin; he did not receive thrombolysis. Diagnosis of myocardial infarction was confirmed with a peak CK estimation of 2489 IU l⁻¹.

He made an uneventful recovery, and prior to discharge underwent an exercise stress test following the Modified Bruce protocol. This was classed as 'borderline positive' demonstrating upsloping ST segment depression to a maximum of 2 mm in lead V₂. He reached a maximum heart rate of 167 beats min⁻¹.

To our knowledge this patient has remained asymptomatic from a cardiological viewpoint, and has received no further investigation or follow up at his own request.

The use of chemotherapy protocols containing such drugs as cisplatin, etoposide, bleomycin and the vinca-alkaloids, in various combinations, for the treatment of germ cell tumours has been associated with the ability to induce myocardial ischaemia or infarction.

This patient received cisplatin and vincristine in the initial course of treatment, but his symptoms appear more directly related to the second combination of dactinomycin, cyclophosphamide and etoposide. There is little evidence to implicate dactinomycin as a vascular toxin. However, as regards cyclophosphamide treatment, although high doses have been associated with cardiomyopathy, any ECG abnormalities or elevation of cardiac enzymes which may occur during or after cyclophosphamide infusion are thought to be secondary to myocardial necrosis rather than any localized vascular events. This has been demonstrated at autopsy.

Several reports implicate cisplatin and vincristine in the development of myocardial infarction or ischaemia, but there is limited evidence to indicate that etoposide may be cardiovascularly toxic. In fact Scharwzer et al. suggested that etoposide had no such effect. The patient in their report continued treatment with etoposide for 14 months following a myocardial infarction which occurred during the treatment protocol containing bleomycin and etoposide. They proposed that the cardiovascular effects were caused by the combinations of the two agents rather than any individual effect. However, Schecter et al. reported a case of myocardial infarction in a 27-year-old female receiving etoposide treatment as a sole agent for persistent Hodgkin’s disease. On rechallenging with this therapy following recovery from the MI, she developed severe hypotension and an ECG demonstrated new lateral T wave inversion indicative of ischaemia. They proposed that the infarction was