by T.L.C.) from abnormal cells contained about six times as much $^{14}$C-palmitate after five days in culture as did that from control cells.

Addition of L-carnitine to the cultures (0·2 g/l of medium) did not modify the enhanced rate of incorporation of $^{14}$C-palmitate into triglyceride by the abnormal cells.

## Comment

The principal clinical features in this patient, ichthyosis and electromyograph abnormalities, may both be related to a defect of lipid metabolism which has led to excessive accumulation of intracellular triglyceride.

Lipids probably play an important part in normal keratinization, and excessive lipid deposition was seen in the keratinizing zone in our case. Furthermore, our patient showed abnormal amounts of lipid droplets in most of the tissues examined, suggesting a generalized defect of lipid metabolism.

The accumulation of apparently normal triglyceride in her cells without a gross excess of cholesterol, the normal serum bile acid concentration, and the absence of hepatomegaly make it unlikely that this patient had cholesterol ester storage disease. Similarly, the absence of lysosomal membranes surrounding the lipid droplets and the presence of normal acid-lipase activity in granulocytes excluded a variant form of Wolman's disease, an inherited disorder of lysosomal lipase activity usually fatal in childhood and rarely seen in adults.

The β-lipoprotein abnormality found in this patient is probably secondary to a defect of intracellular lipid metabolism since fibroblasts continue to show abnormal lipid inclusions when subcultured repeatedly in medium containing normal lipoproteins. Fibroblasts are not known themselves to synthesize β-lipoprotein. A specific defect of triglyceride or fatty acid metabolism at the cytoplasmic level is likely in this patient, and our initial findings suggest impairment either of cytoplasmic lipase activity or of fatty acid transport into mitochondria.

A lipid storage myopathy due to carnitine deficiency was described by Engel and Angelini in 1973. The patient we studied was a vegetarian obtaining little or no carnitine from her diet, so the possibility of defective carnitine biosynthesis leading to impaired transport of fatty acids into mitochondria was considered. This diagnosis was not supported because plasma levels of carnitine were normal and there was no effect on lipid accumulation when L-carnitine was added to fibroblasts in vitro.

Defective carnitine-palmityl-transferase activity could explain our preliminary findings with cultured fibroblasts. Such a lesion was recently shown in a patient with episodic muscle cramps and myoglobinuria (Di Mauro and Di Mauro, 1973), and if confirmed in our case would make a trial of dietary therapy with medium-chain triglyceride worthwhile.

We thank the many colleagues both at Northwick Park Hospital and other hospitals, including Mrs. J. E. Richmond, Dr. G. W. Fenton, Dr. D. S. Smith, Dr. A. Smithies, Dr. B. Lewis, Dr. A. C. Onitiri, Dr. R. D. Cohen, Dr. S. Barnes, Dr. D. Patrick, Dr. M. Ashwell, Dr. P. K. Tubbs, and Dr. A. Lawson who helped us to investigate this patient.

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# Syncopal Attacks as Symptom of Severe Coronary Artery Disease

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*British Medical Journal*, 1975, **1**, 555-556

Syncope is well recognized as a symptom in cardiac disease in association with various arrhythmias (ventricular fibrillation, atrioventricular block, and sinoatrial block), aortic stenosis, hypertrophic obstructive cardiomyopathy, and myocardial infarction. Its association with angina is less well recognized but was noted in original descriptions of angina by Herberden. Gallavardin (1922) and more recently Chiche (1972) described several patients with "syncope anginosa," some with valvular heart disease but also a few with ischaemic heart disease. We report two cases in which syncopal attacks were associated with severe coronary artery disease as shown by coronary arteriography.

## Case 1

A 53-year-old bricklayer was admitted to hospital as an emergency case, having collapsed on his way to work. He was unconscious for a short period. On admission the E.C.G. showed sinus rhythm. He remembered that he had stopped walking up a hill on account of chest tightness immediately before falling unconscious. Further questioning disclosed that he had suffered from typical angina pectoris for some two months before this event. The chest discomfort was always related to exertion, such as walking up a steep hill. While in hospital he had a further syncopal episode. This occurred when he stood up suddenly, having been sitting in a warm room in direct sunlight. Initially no pulse was noted but a

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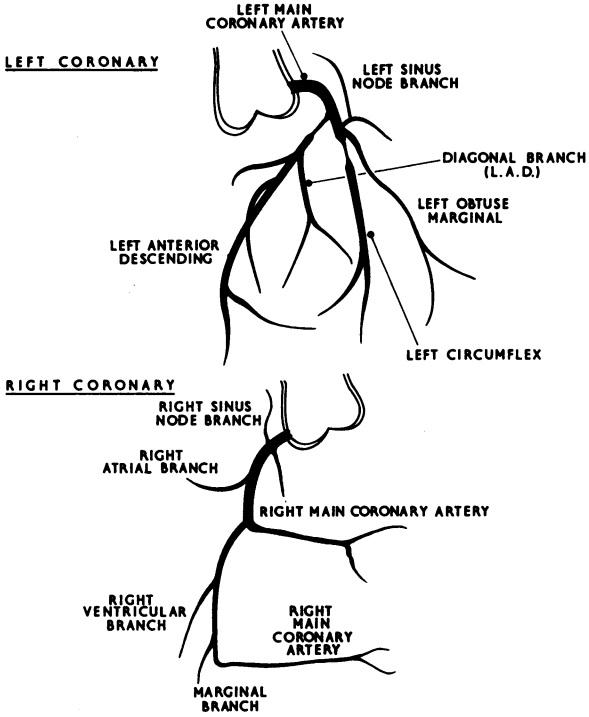


FIG. 1.—Case 1. Left antero-oblique projection of coronary arteries showing major stenoses in proximal parts of left anterior descending and circumflex arteries. Right coronary artery is small in calibre.

subsequent E.C.G. showed atrial fibrillation. He was unconscious for a short time only. He was referred for further investigation.

Examination showed a healthy, well-built man with xanthelasma on both eyelids. Pulse was regular, blood pressure was 90/70 mm Hg, and heart sounds were normal. The resting E.C.G. and chest *x*-ray picture were normal. Six months previously routine blood tests had shown raised serum cholesterol levels and he had been treated with clofibrate.

At cardiac catheterization the left ventriculogram was normal and left ventricular end-diastolic pressure was not raised. Coronary arteriography (fig. 1) showed major stenoses of the left anterior descending artery and left circumflex artery close to their origins. Immediately after the procedure the patient complained of increasing retrosternal pain associated with hypotension and bradycardia. The E.C.G. showed the monophasing potentials of Prinzmetal's variant angina in leads II, III, and aVF with reciprocal changes in anterior precordial leads. He was transferred to the coronary care unit for monitoring, and two hours later, having transiently developed complete heart block, he suffered ventricular fibrillation for which the usual resuscitative measures were unsuccessful. Post-mortem examination confirmed severe stenoses of the left anterior descending and circumflex arteries without evidence of thrombosis. The right coronary artery was small in calibre. Microscopy did not show frank infarction but widespread focal anoxic changes were seen.

## Case 2

A 39-year-old railwayman was referred from another hospital with a six-month history of increasing angina pectoris. The chest tightness was retrosternal with radiation to the jaw. Initially it was related only to severe exertion—for example, running after a bus—but subsequently he had several episodes at rest. At times he had noted light-headedness when he walked too quickly, not always associated with anginal pain. While awaiting admission for investigation he collapsed after a period of moderate exertion and was unconscious for an unknown length of time. An E.C.G. some 30 minutes later showed sinus rhythm and changes of an old anteroseptal myocardial infarction.

Examination showed a thin, muscular man with no stigmata of hyperlipoproteinaemia. Pulse was regular, blood pressure was 95/65 mm Hg, and heart sounds and chest *x*-ray appearances were normal. Fasting blood tests showed raised serum cholesterol and triglyceride levels. At cardiac catheterization left ventricular function, as assessed by angiography, was moderately reduced with some anterolateral dyskinesia. The left ventricular end-diastolic pressure was slightly raised at 14 mm (post "a" wave) and left ventricular dp/dt was 850 mm Hg/sec. Coronary arteriography showed a major stenosis of the left anterior descending artery at its origin, reduced flow in the left circumflex artery, and a greater-than-50% stenosis of the right main coronary artery (fig. 2).

Early surgery was advised, and under cardiopulmonary bypass triple saphenous vein aortocoronary grafts were inserted. The arteriographic findings were confirmed at operation. His progress was satisfactory six months later.

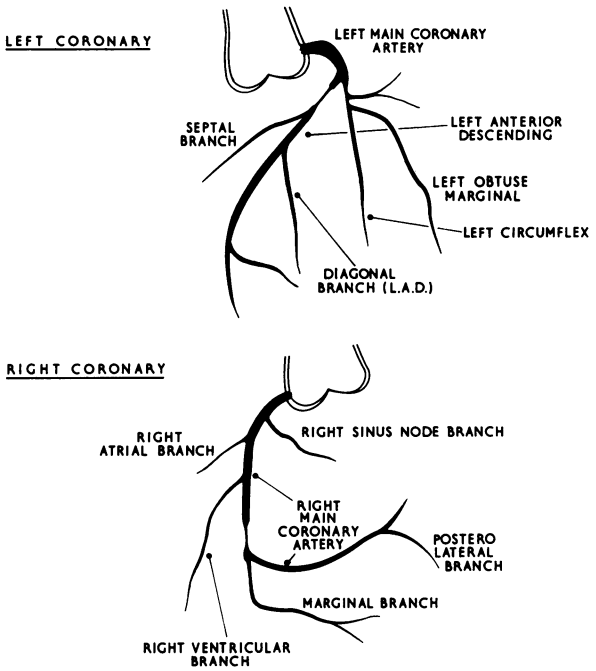


FIG. 2.—Case 2. Left antero-oblique projection of coronary arteries showing major stenoses in left anterior descending and right main arteries. Left circumflex artery is small in calibre.

## Comment

The clinical histories of these two patients were similar. Both had recent-onset anginal pain associated with syncopal attacks. One episode was associated presumably with atrial fibrillation. The most likely explanation of these syncopal attacks is that they are secondary to arrhythmias, possibly an intense bradycardia analogous to the bradycardia seen during coronary arteriography. The alternative explanation—that is, failure of the heart to respond to an increased output demand—cannot be disproved. It seems likely that the reduction in calibre of the major coronary arteries would make sudden increases in myocardial blood flow difficult to achieve. In relation to this suggestion it is interesting to note that both patients had low blood pressure with a reduced pulse pressure. This is often associated with a low cardiac output—for example, after myocardial infarction.

The similarity of the arteriographic pattern in these cases to those described in cases of Prinzmetal's variant angina, and the development of this E.C.G. pattern in one of the cases after coronary arteriography, suggests a relationship between syncope and Prinzmetal's angina. This was reported by Levi and Proto (1973), who described episodes of ventricular arrhythmia and syncope in two out of seven patients with variant angina. In one case coronary arteriography confirmed the existence of proximal stenosis of the anterior descending coronary.

These cases also raise the question of the possible relationship to the common occurrence of sudden death associated with severe coronary atherosclerosis. Coronary occlusion is frequently not observed at necropsy and fresh coronary thrombi are found in only a few cases (Moritz and Zamcheck, 1946; Spain and Bradess, 1960; Adelson and Hoffman, 1961; Speikerman *et al.*, 1962). It is at least possible that many of these cases are due to the same mechanism responsible for syncopal attacks.

The occurrence of syncopal attacks in association with angina should raise the suspicion of severe atheroma, particularly of the left coronary artery, whether involving the main artery itself or both of its branches. This represents a life-threatening condition for the patient but one which is potentially remediable by aortocoronary bypass grafting. Cohen *et al.* (1972) documented the high mortality from coronary angiography in patients with stenosis of the left main artery, which is an equivalent situation to that described here, and caution is therefore required in the performance of the angiography. The first case described here points to the dangers of delay in operating on patients with critical stenosis who develop symptoms after coronary angiography.

We wish to thank the referring physicians. Aortocoronary bypass surgery was carried out in case 2 by Mr. Philip Caves. Requests for reprints should be sent to Dr. J. B. Irving.

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