

## Heart abnormalities in IDDM

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Following the discovery of insulin in 1922 it became clear that patients with insulin-dependent diabetes mellitus (IDDM) did not have a normal life expectancy, and the era of coma as the central problem of diabetes gave way to the era of complications. The pathophysiology of complications affecting the retina, kidney, and nervous system has been extensively studied, and detailed protocols devised for the early detection, investigation and treatment of these problems.

Cardiovascular disease has received much less detailed investigation. Advances for non-diabetic patients in the medical and surgical treatment of coronary heart disease and its risk factors have greatly improved the prognosis, and the time is ripe for a new era of cardiovascular research in people with diabetes. This article reviews current knowledge of heart disease in IDDM.

### *Epidemiology*

Detailed epidemiological studies including Framingham have defined an excess of symptomatic coronary heart disease, myocardial infarctions and congestive cardiac failure in the diabetic population. These studies have identified middle-aged women on treatment with insulin as a particular high-risk group for congestive cardiac failure. Unfortunately many of these studies have categorised people with diabetes according to treatment type (often 'insulin-treated' or 'non-insulin-treated'), and there is a need for detailed epidemiological studies according to type of diabetes (insulin-dependent or non-insulin-dependent (NIDDM)

with further detailed analysis of patients with NIDDM according to treatment to answer questions about the possible adverse cardiovascular effects of insulin or sulphonylureas.

### *Coronary heart disease*

Information about coronary heart disease has been obtained from post-mortem analysis of coronary lesions, non-invasive stress testing using exercise electrocardiography, and coronary arteriography. Many studies have included patients with both IDDM and NIDDM, or have included only small numbers of IDDM patients so that sub-group analysis was not possible. Studies have shown that people with IDDM have an increased prevalence of coronary disease, which often affects multiple vessels, and is diffuse within an affected artery.

When patients are defined according to renal protein excretion as having normoalbuminuria, microalbuminuria, or macroproteinuria, then using epidemiological studies and exercise electrocardiography patients with normal albumin excretion appear to have little excess cardiovascular disease, with the most severe abnormalities present in patients with macroproteinuria, even when allowing for the effects of hypertension which itself is a risk factor for cardiovascular disease [1]. If these findings are confirmed, this would raise the possibility of targeting screening for coronary heart disease and multiple-risk factor intervention at this group of patients.

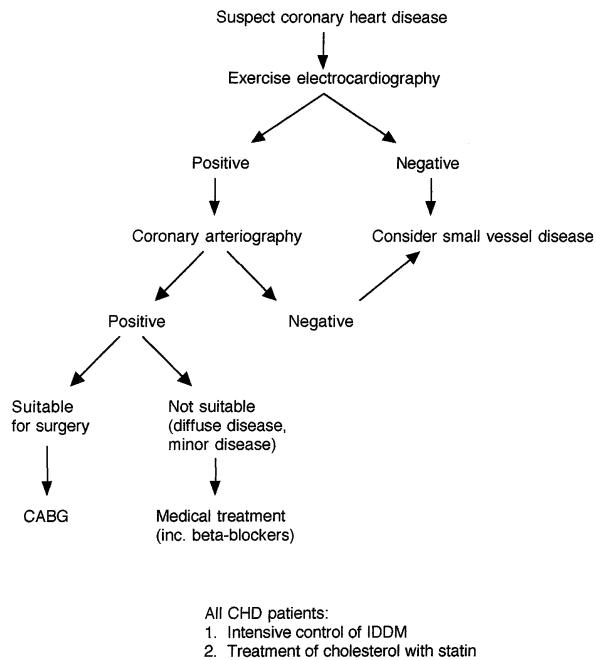
### *Treatment of coronary heart disease (Fig. 1)*

In the patient with IDDM, three different and complementary strategies are available to treat coronary heart disease [2]. Firstly, data from the Diabetes

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*Abbreviations:* IDDM, Insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus.



**Fig 1.** Investigation and treatment of coronary heart disease in IDDM. CABG, coronary artery bypass graft

Control and Complications Study (DCCT) study [3] has shown that in addition to the significant reduction in retinopathy and nephropathy there was a non-significant reduction in cardiovascular end-points in the intensively treated group. The group as a whole was young, and there was a relatively small number of cardiovascular events, but it seems unlikely that a study of this size will be repeated in a higher risk group, and this study suggests that intensive treatment of IDDM improves cardiovascular prognosis.

Secondly, patients can be treated by reduction in cardiovascular risk factors. Post-hoc analysis of diabetic patients in the 4S Study [4] shows that reduction in cholesterol using simvastatin was associated with a reduction in cardiovascular mortality. Most of these patients had NIDDM, and it is incumbent upon those designing future trials of cardiovascular risk factor reduction to include patients with IDDM.

Thirdly, patients who have developed symptoms of chest pain or breathlessness suggestive of coronary disease should undergo detailed investigation at an early stage to identify patients who would benefit from surgical treatment.

### Myocardial infarction

Thrombolytic therapy reduces mortality following myocardial infarction, and the reduced mortality is shared by patients with diabetes, although few patients with IDDM have been studied. In early studies patients with proliferative retinopathy were excluded because of a theoretical risk of retinal haemorrhage.

This has not been confirmed in clinical practice, and patients with the triad of diabetic retinopathy, diabetic nephropathy and myocardial infarction should not be denied thrombolytic therapy. Similarly, beta-blockers are of proven benefit and should be widely used post myocardial infarction despite any theoretical risk of masking the symptoms of hypoglycaemia, or worsening of the lipid profile.

Until recently the management of hyperglycaemia at the time of myocardial infarction was not of proven prognostic benefit. Data from the DAGAMI study [5] in NIDDM patients suggests that treatment with intravenous insulin to totally normalise blood glucose, with subsequent basal bolus insulin therapy, is associated with a reduction in mortality. The study design has been heavily criticised, and any potential lessons for IDDM patients are not yet clear.

### Other forms of heart disease

In addition to the burden of coronary heart disease there is compelling evidence for the existence of a specific heart disease of diabetes in IDDM based on non-invasive studies and histological data [6]. It is not clear, however, whether the relatively minor abnormalities on non-invasive testing progress to cause severe ventricular dysfunction. It has been suggested that the coexistence of this specific heart disease of diabetes affecting the left ventricle may be one possible explanation for the excess mortality which is seen following myocardial infarction in patients with diabetes [6].

The exact clinical significance of the cardiac diabetic autonomic neuropathy is also unclear. Studies have suggested an excess of silent myocardial ischaemia and silent infarction in diabetic patients, and this has been attributed to autonomic neuropathy. However, in non-diabetic patients many episodes of myocardial ischaemia are painless, as are several myocardial infarctions, so diabetic autonomic neuropathy cannot be the whole explanation.

### Conclusions

Coronary heart disease remains the commonest cause of premature death in IDDM patients, possibly interacting with the specific heart disease of diabetes and diabetic autonomic neuropathy. Patients with microalbuminuria and macroproteinuria are at particular risk, and more studies of the pathophysiology of coronary heart disease in IDDM patients are urgently required.

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