Increased plasma lipoprotein (a) concentrations in Behcet's disease and its relation to vascular events

Behcet's disease, which is characterised by oral and genital ulcerations and eye inflammation, was discovered by Hulusi Behcet in 1937. Other features include arthritis, thrombophlebitis, neurological abnormalities, and skin lesions. Increased incidence of vascular manifestations has been reported in patients with Behcet's disease and may constitute one of the most important causes of mortality and morbidity in these patients. The disease is characterised by a relapsing inflammatory process of unknown aetiology.

Lipoprotein (a) (Lp(a)) is a cholesterol rich plasma lipoprotein that has emerged as an important risk factor for development of coronary artery disease and stroke. Lp(a) could contribute to lipid deposition on arterial walls. Moreover, the recent finding that apo(a) is analogous to plasminogen suggests the possibility that Lp(a) could be the link between thrombosis and atherosclerosis.1 2

The aim of this study was to measure the plasma concentrations of Lp(a) in patients with Behcet's disease and to find relationships between Lp(a) concentrations and clinical findings including disease activity, ocular involvement, articular symptoms, skin lesions, neurologic involvement, and other lipid parameters. The study included 27 patients with Behcet's disease (15 men and 12 women; mean (SD) age 33.1 (10) years, range 19–65 years) and 17 healthy control subjects (10 men and 7 women; mean age 33.5 (12.1) years, range 20–59 years). The groups were matched for factors influencing lipoprotein concentrations such as diet, body mass, and exercise.

Oral aphthous lesions were found in all the patients, recurrent disease. Ocular involvement was seen in 14 patients, genital ulcerations in 14 patients, and skin lesions (erythema nodosum, pyoderma, folliculitis, skin ulcers, etc) in 12 patients. Arthritis or arthritis-like joint involvement occurred in 12 patients, and neurologic in three patients. At the time of the study, the patients were being treated with either colchicine (n = 5) or non-steroid anti-inflammatory drugs (n = 10), or both (n = 8), the remaining four patients receiving no systemic medication.

Serum total cholesterol was measured by a cholesterol oxidase enzymatic method, triglycerides by a glycerol oxidase enzymatic method, and high density lipoprotein cholesterol (HDL-C) by a cholesterol oxidase enzymatic method in supernatant after precipitation with phosphotungstic acid–magnesium chloride. Apolipoproteins AI and B were determined by an immunosassay method (Sera-Pak Immuno Apo AI (code no. 6821)/Apo B (code no. 6822), Ames, Canada). Low density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula. Lp(a) was measured using commercial anti-apo(a) polyclonal capture enzyme linked immunosorbent assay (TintElize Lp(a), catalogue no. 610210; Biopool AB, Umeå, Sweden) according to the manufacturer's instructions. An intra-assay coefficient of variation of 6.1% was obtained at the 31 mg/dl concentra-
tion of Lp(a) reference plasma (Biopool, catalogue no. 610142, n = 10).

Data were expressed as mean (SD). Lp(a) concentrations and other lipid parameters were compared by Mann Whitney U test, because of the skewed distributions of these values. Disease duration of the patients with Behcet's disease, cholesterol, triglyceride, LDL, HDL, Apo AI, and Apo B were compared with Lp(a) concentrations using regression analyses.

The results are summarised in table 1. Plasma Lp(a) concentrations in patients with Behcet's disease were significantly higher than in the healthy controls. There were no significant differences in the concentrations of total cholesterol, LDL-C, HDL-C, triglycerides, and apolipoproteins AI and B between patients and controls. As shown in table 1, plasma Lp(a) concentrations were not influenced by disease activity, but were affected by the presence of ocular, neurological, and articular involvement and skin lesions. Also, no correlation was observed between plasma Lp(a) concentrations and plasma concentrations of cholesterol, HDL-C, LDL-C, Apo AI, and Apo B, except for triglycerides (r = 0.468, p < 0.01).

Atherogenic, thrombogenic, and inflammatory vascular events increase in patients with Behcet’s disease. High concentrations of Lp(a) (> 30 mg/dl) increase the risk of atherogenic and thrombogenic events. Scott estimated that at plasma Lp(a) concentrations of 30 mg/dl, cellular plasmiminogen binding of Lp(a) is reduced 20%, thereby decreasing cell fibrinolysis and promoting a procoagulant state.3 Previously, Orem and colleagues from Turkey also reported that fluctuations of plasma Lp(a) concentrations with disease activity may be a contributing risk factor in the development of thrombogenic complications in patients with Behcet's disease. In addition, in the present study, significant relations were found between Lp(a) concentrations and neurologic, articular, and ocular involvements and skin manifestations within the study group. These findings may be related to vascular manifestations. Also, Lp(a) concentrations were correlated with triglyceride concentrations. This study shows that plasma Lp(a) concen-
trations increase in patients with Behcet’s disease. Lp(a) may therefore play a role in the thrombogenic and atherosclerotic events associated with this disease.

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Table 1 Mean (SD) Lp(a) concentrations in patients with Behcet’s disease and controls, and their relation to the presence or absence of clinical findings

<table>
<thead>
<tr>
<th>Group</th>
<th>Lp(a) (mg/dl)</th>
<th>Presence (%)</th>
<th>Absence (%)</th>
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<tbody>
<tr>
<td>Controls (n=27)</td>
<td>16.9 (12.1)</td>
<td>(median 10.7)</td>
<td>17.6 (4.4)</td>
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<tr>
<td>Behcet’s disease patients (n=27)</td>
<td>27.2 (21.1)*</td>
<td>(median 20.3)</td>
<td>37.3 (10.4)</td>
</tr>
</tbody>
</table>

Significantly different from the other group: *p < 0.05; **p < 0.01 (Mann-Whitney U test).

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10 Coronary angioplasty is like going to the dentist
B Meier
May 2000;83:491–2 (Editorial)
Diabetic cardiomyopathy can be a major complication of diabetes. This complication is not only present in established diabetes but also in prediabetes. Increased diastolic stiffness develops early in experimental diabetic animals which is associated with interstitial accumulation of connective tissue. The Otsuka Long-Evans Tokushima Fatty (DM) strain of rat was established as an animal model of congenital diabetes, manifesting stable clinical and pathological features that resemble human non-insulin dependent diabetes mellitus (NIDDM). In our previous study we found alteration in left ventricular diastolic function and accumulation of myocardial collagen in prediabetic rats. Troglitazone, an insulin sensitising thiazolidinedione, improves metabolic deterioration in diabetic animal models, obese subjects, and patients with NIDDM. The drug has an acute effect on cultured cardiac myocytes, on isolated rat hearts, and prevents high glucose induced insulin resistance in cultured rat fibroblasts. Our study aimed to examine the long term effects of troglitazone on myocardial collagen content using histopathological methods in prediabetic rats.

Male DM rats and age matched male non-DM rats were randomly divided into two groups, respectively: (1) treated DM (n = 10); (2) untreated DM (n = 10); (3) treated non-DM (n = 10); (4) untreated non-DM (n = 10). Rat chow (Oriental Yeast Co, Tokyo, Japan) with or without 0.2% troglitazone (Sankyo, Japan) was given from the age of 5 weeks up to 15 weeks. Before and after treatment, blood sampling for fasting blood glucose, fasting plasma total cholesterol (cholesterol oxydase-peroxydase method), and fasting plasma triglyceride (glycerokinase-glycerol-3-phosphoxydase method) were obtained after an overnight fast. An oral glucose tolerance test (OGTT), plasma insulin concentration (enzyme linked immunosorbent assay method, Levis insulin kit, Japan), plasma alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were measured at 15 weeks of age.

There were no abnormal values for ALT or AST in any of the four groups. There was no significant difference in fasting blood glucose between treated and untreated groups. Troglitazone treatment decreased fasting plasma triglyceride in diabetic rats (untreated 0.64 (0.17) mmol/l v treated 0.26 (0.18) mmol/l, p < 0.001). At 15 weeks of age there was significant differences in two hour blood glucose on OGTT (mmol/l) and plasma insulin concentration (ng/ml) between untreated DM (10.4 (1.5) mmol/l, 8.1 (1.5) ng/ml) and untreated-non DM (6.1 (0.4) mmol/l, 3.8 (2.1) ng/ml, p < 0.001, respectively). Troglitazone treatment improved glucose tolerance and insulin sensitivity of diabetic rats (two hour blood glucose on OGTT 7.7 (1.1) nmol/l v untreated DM, p < 0.005; plasma insulin concentration 3.2 (0.4) ng/ml v untreated DM, p < 0.001). In both the treated and untreated groups there was no dilation or hypertrophy observed on heart excisions. Troglitazone treat-
Emergency DDD pacing using a single lead, balloon tip catheter

A 74 year old woman presented with cardiogenic shock and a ventricular septal defect (VSD), four days after an undiagnosed inferior myocardial infarction. An infero-apical VSD was repaired using a 4 × 3 cm Dacron patch during emergency cardiopulmonary bypass. Despite postoperative ventilation, balloon pump, and inotropic support she remained hypotensive and oliguric on the third postoperative day. In addition, inappropriate sinus bradycardia resulted in frequent ectopy and eight episodes of ventricular tachycardia/fibrillation, requiring DC cardioversion.

Ventricular demand (VVI) pacing via epicardial temporary pacing leads increased heart rate, but did not improve blood pressure or urine output. Neither VVI pacing, nor intravenous loading with amiodarone, suppressed the ventricular arrhythmia.

Dual chamber (DDD) temporary pacing was achieved using a single lead balloon flotation catheter (panel A: the two ventricular, three atrial and single indifferent superior vena cava (SVC) electrode positions are marked. Inset: 1.0 ml air filled balloon to facilitate “flow directed” catheter positioning.) This electrode catheter allows atrial pacing in DDD mode by overlapping biphasic impulses (OLBI, Biotronik) via a pair of non-contact atrial electrodes. Fluoroscopic screening was used to optimise electrode position (panel B). Reliable DDD pacing using an external generator (Eikos SLD, Biotronik) was maintained at 100 beats per minute for five days with dramatic clinical improvement. There was a 24 mm Hg rise in mean arterial pressure (panel C) enabling withdrawal of inotropic support, recovery of renal function, and a steady clinical improvement. In addition, the ventricular arrhythmia was completely suppressed apart from two further episodes of ventricular tachycardia provoked by testing ventricular thresholds in VVI mode.


Commentary
Thiazolidinedione agents called “glitazones” are being developed for the treatment of non-insulin dependent diabetes mellitus (NIDDM). These drugs stimulate peroxisome proliferator activated receptor-γ (PPAR-γ), an action distinct from those of existing sulfonylurea and biguanide drugs. This report shows that troglitazone, a member of this new class, exerts a myocardial anti-fibrotic action in a genetic animal model of NIDDM, at an early stage of disease progression. The mechanism of this novel action is unknown but may be relevant to the pathophysiology and treatment of diabetic cardiomyopathy.

G F BAXTER
Associate Editor