Coronary risk factors in people from the Indian subcontinent living in West London and their siblings in India


Summary
Several reports have shown that migrants from southeast Asia tend to have an increased risk of coronary heart disease when settled in their new country. We compared coronary risk factors in a randomly selected group of 247 migrants from the Indian subcontinent of Punjabi origin living in West London and 117 of their siblings living in the Punjab in India.

The West London cohort had a greater body mass index (p<0.001), systolic blood pressure (p=0.0087), serum cholesterol (p<0.001), apolipoprotein B (p<0.001), lower high-density lipoprotein cholesterol (p<0.05) and higher fasting blood glucose (p<0.05) than their siblings in the Punjab. Insulin sensitivity, derived from the homeostatic assessment mathematical model, was lower in men in West London than in their counterparts in India (p<0.05). Indians in West London had lower β cell function than those in the Punjab (p<0.001). Serum lipoprotein (a) concentrations were similar in both the West London and Punjab population, but were significantly higher (p=0.01) than those of white European populations in the UK.

Increases in serum cholesterol after migration from India lead to increased coronary risk conferred by high serum lipoprotein (a) concentrations and greater insulin resistance. Such between-country comparisons are an important means of establishing the importance of coronary risk factors.

Lancet 1995; 345: 405-09

See Commentary page 401

Introduction
Several reports show that migrants from the Indian subcontinent have an increased risk of coronary heart disease (CHD). Sometimes their CHD risk rises above that of the society to which they have migrated despite the fact that their serum total cholesterol is similar to or lower than that of the indigenous population. Other coronary risk factors such as cigarette smoking are also similar. McKeigue and co-workers have suggested that the excess mortality rates of CHD that occur in an immigrant Indian population, which cannot be fully explained on the basis of conventional risk factors, may be partly due to decreased insulin sensitivity, which may be the result of genetic differences. However, even insulin sensitivity cannot fully account for the increased coronary mortality in Indians.

Serum lipoprotein (a) (Lp(a)) is another inherited CHD risk factor that has not been investigated in migrant Indians. Serum Lp(a) is largely unaffected by diet or drugs and is a particular risk factor when associated with increased serum low-density-lipoprotein cholesterol. Apolipoprotein (a), which is a constituent protein of Lp(a), has considerable homology with plasminogen and may interfere with fibrinolysis. Furthermore this protein is retained in the arterial wall and thus contributes to atherogenesis.

There are scanty data about the prevalence of CHD in India, but in view of the physical geography, size, and cultural diversity of the country there will inevitably be variations. The predominantly rural population in India is, however, likely to have a lower prevalence of CHD than that seen in the UK. The reports of increased mortality in Indian migrants to the UK from such communities reflect the interplay of the newly acquired nutritional or emotional environment against a background of genetic susceptibility.

Subjects and methods
UK
We carried out our study in the Northcote ward of Southall in West London (population 12,858), where 83% (n=8764) of residents in the 1991 census came from the Indian subcontinent. We assessed 485 subjects with Indian surnames who were randomly selected from the electoral register. Fasting blood samples were taken on-site and analysed in Manchester.

Siblings in India
One-third of participants in West London gave sufficiently detailed information for one or more siblings still living in India to be contacted. These siblings were investigated in a similar way to the West London cohort by a team of local investigators (GSW, ISA, YC). Recruitment of siblings was limited to the state of Punjab in India. In India the study was coordinated from the
Department of Cardiology at the Post Graduate Institute of Medical Education and Research, Chandigarh. A field team of doctors and technicians went to a specific area or village in a district after initial postal confirmation of assent for the study. Fasting blood samples were taken on-site and transported at 4°C to the laboratory in Chandigarh.

Protocol
All subjects had a clinical examination. A recording was made of the blood pressure, and patients completed a supervised bilingual questionnaire about symptoms of CHD, neuroses, and environmental stresses. Blood pressure was measured after the subject had been seated for 5 min. Blood samples were taken after an overnight fast for the determination of serum cholesterol, triglycerides, high-density-lipoprotein (HDL) cholesterol, apolipoprotein B (apo B), Lp(a), insulin, and blood glucose. The UK and India blood was centrifuged on the day of collection and serum separated into aliquots. Before freezing aliquots, we used one of them to isolate HDL using the same batch of reagents for heparin-MnCl₂ precipitation in India and Manchester. Both laboratories participated in external quality-assurance schemes for serum lipid determinations; their performance was satisfactory. Aliquots of the same quality-control material used in Manchester were sent to India for within-batch analysis and showed no significant differences in performance between the laboratories for any of the variables. There was close agreement between values; mean (SE) cholesterol values measured in Chandigarh and Manchester were 5.3 (1.2) and 5.0 (1.1) mmol/L, respectively, and median (range) triglycerides were 2.10 (2.0-2.63) and 2.15 (1.8-3.3), respectively.

Laboratory methods
The frozen samples from West London and Chandigarh were transported to Manchester on dry ice. Cholesterol in serum, and HDL, serum triglycerides, insulin, apo B and Lp(a) were measured in the Department of Medicine in Manchester. To ensure that there were no changes in the lipid concentrations because of transportation, another aliquot of serum was used to analyse samples with similar analytical methods in Chandigarh. Site visits to the laboratory in India were done by one of us (DB). Reagents and standards used for analysis were obtained in the UK and were shipped to India with appropriate precautions. Reagents and standards used for analysis were obtained in the UK and were shipped to India with appropriate precautions. Both laboratories participated in external quality-assurance schemes for serum lipid determinations; their performance was satisfactory. Aliquots of the same quality-control material used in Manchester were sent to India for within-batch analysis and showed no significant differences in performance between the laboratories for any of the variables. There was close agreement between values; mean (SE) cholesterol values measured in Chandigarh and Manchester were 5.3 (1.2) and 5.0 (1.1) mmol/L, respectively, and median (range) triglycerides were 2.10 (2.0-2.63) and 2.15 (1.8-3.3), respectively.

Serum and HDL-cholesterol were measured by a CHOD-PAP method and triglycerides by a GPO-PAP method, both on a discrete analyser. Apo B was measured by rate immunonephelometry on the Beckman Array (Beckman, Palo Alto, USA). Serum Lp(a) was measured by a two-site immunoradiometric assay (Pharmacia, Milton Keynes, UK) calibrated in the Manchester laboratory against the protein concentration of a preparation of Lp(a) isolated from human tissues. Serum insulin was determined by an assay based on the modification of the double-antibody method of Morgan and Lazarus and validated before use by the substitution of standards with the WHO first international reference preparation of human insulin and through human-derived control sera (Lyphochek, Bio Rad Laboratories, Watford, UK). Blood glucose was analysed by the same glucose oxidase method in India as in the UK.

We obtained a measure of insulin sensitivity and β-cell function from fasting blood glucose and insulin by the homeostasis assessment mathematical model (HOMA). The calculations are based on the assumption that control of plasma glucose and insulin concentrations in the fasting state is determined by a self-contained feedback loop that involves the liver, β-cells, and both insulin-sensitive and insulin-insensitive tissues. Insulin sensitivity is expressed as a percentage of that in a healthy, lean reference population of European descent living in the Oxford area who were assigned a value of 100% for insulin sensitivity and β-cell function by the inventors of the method.

Table 1: Clinical characteristics, serum lipids, apolipoproteins, and blood pressure in Indians living in West London and their siblings in the Punjab

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>West London</th>
<th>Punjab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>46.0 (10.6)</td>
<td>44.4 (9.4)</td>
<td>45.6 (9.4)</td>
<td>45.8 (9.9)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 (5.2)</td>
<td>22.9 (4.7)</td>
<td>27.4 (4.9)</td>
<td>27.2 (4.7)</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>6.5 (1.4)</td>
<td>4.9 (1.1)</td>
<td>6.2 (1.2)</td>
<td>5.1 (1.0)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.12 (0.45)</td>
<td>1.21 (0.43)</td>
<td>1.16 (0.42)</td>
<td>1.34 (0.39)</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>2.10 (2.06)</td>
<td>1.66 (1.71)</td>
<td>1.49-1.95</td>
<td>1.45-2.01</td>
</tr>
<tr>
<td>Apo B (mg/dl)</td>
<td>103.6</td>
<td>62.5</td>
<td>91.8</td>
<td>65.5</td>
</tr>
<tr>
<td>Lp(a) (mg/dl)</td>
<td>18.8</td>
<td>17.4</td>
<td>20.4</td>
<td>18.9</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>146 (23)</td>
<td>132 (22)</td>
<td>143 (28)</td>
<td>142 (23)</td>
</tr>
</tbody>
</table>

*P<0.05; †P<0.001; geometric mean and 95% CI. BM=body mass index.

Statistical analysis
Data from questionnaires, clinical examination, and laboratory determinations were stored on a computer database at the University of Manchester. Statistical analyses were performed with a Statistical Software Package. Serum triglycerides, Lp(a), insulin, β-cell function, and insulin sensitivity had log normal distributions and are presented as geometric mean with 95% CI. Group means were compared by t test or analysis of variance on actual data for normally distributed variables and on log-transformed data for log-normal variables. The association between variables was tested by Pearson’s correlation coefficients.

Results
West London population
Of the 485 individuals approached in Southall, 390 agreed to participate in the study (response rate 81%). Complete data were available for 376 participants. One individual who was profoundly hyperlipidaemic (serum cholesterol >12 mmol/L; triglycerides >30 mmol/L) was excluded from the analysis. Since all Indian siblings were from the Punjab, all comparisons are restricted to West London subjects who were originally from the Punjab (n=247; 118 men 129 women). In this Punjabi population 73.7% were Sikhs, 17.8% were Hindus, 6.8% were Muslim, and 1.7% were Christian. The results of the serum lipids and apolipoprotein measurements in the remaining West London population did not differ from the West London cohort who originated from the Punjab.

Siblings in the Punjab
We contacted siblings of 59 West London subjects. There were no differences between these subjects and either the rest of the West London study population or the West London cohort born in the Punjab. On average 2 siblings were contacted for each index subject, so demographic data and blood samples were obtained from 120 siblings from the Punjab. Complete and verifiable data were available on 117 subjects from India (66 men and 54 women), who were the siblings of 59 of the West London sample. 52% were Sikh, 43.1% were Hindu, and 4.6% were Christian.

The mean age of subjects in India and in West London was similar (table 1) and there were no differences in age between the sexes either in India or in West London.

Table 1 shows that men and women from the Punjab had a significantly lower body mass index (kg/m²) than
Table 3: A comparison of serum Lp(a) in Europeans and in Indians living in West London and their siblings in the Punjab

<table>
<thead>
<tr>
<th></th>
<th>West London</th>
<th>Punjab</th>
<th></th>
<th>West London</th>
<th>Punjab</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>118</td>
<td>65</td>
<td></td>
<td>129</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Blood glucose</td>
<td>5·7±1·4</td>
<td>4·5±1·0</td>
<td></td>
<td>5·1±1·2</td>
<td>4·7±0·8*</td>
<td></td>
</tr>
<tr>
<td>Serum insulin</td>
<td>8·4±7·9</td>
<td>6·7±5·4</td>
<td></td>
<td>8·0±7·0</td>
<td>8·9±7·5</td>
<td></td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>45·6</td>
<td>59·8*</td>
<td></td>
<td>47·9</td>
<td>45·3</td>
<td></td>
</tr>
<tr>
<td>β-cell function</td>
<td>86·0</td>
<td>134±11</td>
<td></td>
<td>108±4</td>
<td>156±7</td>
<td></td>
</tr>
</tbody>
</table>

*p<0·05; †p<0·001; ‡geometric mean and 95% CI.

Discussion

To investigate further the similarity of Lp(a) concentrations in the two populations we matched 30 subjects from West London with their siblings in the Punjab who were of the same sex and of similar age (45·7 [9·6] vs 44·6 [8·1]) and carried out paired *t* tests between the two groups for each variable. The Punjab siblings had a lower body mass index (p<0·001), serum cholesterol (p<0·001), and apo B (p<0·001), whereas blood glucose (p=0·069), HDL cholesterol (p=0·55), insulin sensitivity (p=0·12), whereas β-cell function (p=0·55), serum Lp(a) (p=0·11), systolic blood pressure (p=0·13), diastolic blood pressure (p=0·47), and triglycerides (p=0·27) were not statistically different. The only significant correlation observed was between serum Lp(a) of the matched siblings (Pearson’s *r*=0·45; p=0·036) indicating a substantial element of heritability.

Table 2: Blood glucose, serum insulin, β-cell function, and insulin sensitivity in Indians living in West London and their siblings in the Punjab

<table>
<thead>
<tr>
<th></th>
<th>West London</th>
<th>Punjab</th>
<th></th>
<th>West London</th>
<th>Punjab</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>118</td>
<td>65</td>
<td></td>
<td>129</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Blood glucose</td>
<td>5·7±1·4</td>
<td>4·5±1·0</td>
<td></td>
<td>5·1±1·2</td>
<td>4·7±0·8*</td>
<td></td>
</tr>
<tr>
<td>Serum insulin</td>
<td>8·4±7·9</td>
<td>6·7±5·4</td>
<td></td>
<td>8·0±7·0</td>
<td>8·9±7·5</td>
<td></td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>45·6</td>
<td>59·8*</td>
<td></td>
<td>47·9</td>
<td>45·3</td>
<td></td>
</tr>
<tr>
<td>β-cell function</td>
<td>86·0</td>
<td>134±11</td>
<td></td>
<td>108±4</td>
<td>156±7</td>
<td></td>
</tr>
</tbody>
</table>

*p<0·05; †p<0·001; ‡geometric mean and 95% CI.

Table 3: A comparison of serum Lp(a) in Europeans and in Indians living in West London and their siblings in the Punjab

<table>
<thead>
<tr>
<th></th>
<th>West London</th>
<th>Punjab</th>
<th></th>
<th>West London</th>
<th>Punjab</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>118</td>
<td>65</td>
<td></td>
<td>129</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Blood glucose</td>
<td>5·7±1·4</td>
<td>4·5±1·0</td>
<td></td>
<td>5·1±1·2</td>
<td>4·7±0·8*</td>
<td></td>
</tr>
<tr>
<td>Serum insulin</td>
<td>8·4±7·9</td>
<td>6·7±5·4</td>
<td></td>
<td>8·0±7·0</td>
<td>8·9±7·5</td>
<td></td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>45·6</td>
<td>59·8*</td>
<td></td>
<td>47·9</td>
<td>45·3</td>
<td></td>
</tr>
<tr>
<td>β-cell function</td>
<td>86·0</td>
<td>134±11</td>
<td></td>
<td>108±4</td>
<td>156±7</td>
<td></td>
</tr>
</tbody>
</table>

*p<0·05; †p<0·001; ‡geometric mean and 95% CI.

Vol 345 • February 18, 1995

407
living in Africa and those living in the US the incidence of coronary artery disease is less than that seen in caucasians. This is probably because Africans and their descendants have lower LDL cholesterol concentrations than people of European descent. Indians, on the other hand, would appear to have higher Lp(a) and to have the capacity to rapidly acquire the higher LDL cholesterol of Europids on emigrating to a country like Britain. Therefore, diet and lifestyle-induced increases in serum cholesterol in Indians add to the genetic background of a potentially atherogenic and thrombogenic state due to high serum Lp(a).

McKeigue et al have proposed that insulin resistance is an important factor that may explain the increased frequency of coronary artery disease seen in Indians. Our results support earlier investigations showing that Indians are more insulin resistant than Europeans and further suggest that Indians are insulin resistant even before migration. However, this conclusion must be tempered by the knowledge that the European population with which this comparison was made was non-obese. We can, however, draw much stronger conclusions from the comparison of the Indians in Britain and in India and it seems clear from this that there is both a deterioration in insulin resistance and β-cell function associated with migration.

As in other populations, insulin resistance is accompanied by other CHD risk factors such as increased serum triglyceride, low HDL cholesterol, and central obesity. All these factors are more prevalent in Indian immigrants in several geographical locations. Our study contributes to the question of whether South Asians develop insulin resistance before migration or whether they develop it through unaccustomed nourishment afterwards. Decreased insulin sensitivity was present in the Punjabi population who had not migrated. This finding does not neccessarily mean that Indians are genetically predisposed to insulin resistance because Barker and Hales have suggested that a thrifty phenotype possibly develops in response to in-utero nutritional deprivation and that such imprinting may offer protection during chronic undernutrition. These theories have yet to be tested in people from the Indian subcontinent, most of whom have children of smaller birth weight (even in affluent families) and, as adults, generally have a lower body mass index compared with white Europeans. Especially relevant would be the degree of insulin resistance of the children of Indians resident in the UK. Whatever the explanation of the insulin insensitivity in Indians the likelihood that it will be expressed as glucose intolerance and frank diabetes probably increases when their dietary intake of energy and fat increases on migration to countries such as the UK. The apparent deterioration in pancreatic secretory capacity in the migrant Punjabis in this study would also reward further study in this context.

Immigrant men in West London had higher systolic blood pressures than their counterparts in the Punjab. These observations are consistent with earlier findings in Indians migrating to London and remaining in India. As with our study, there was also a relation between body mass index and blood pressure. The inverse relation we found between blood pressure and insulin sensitivity in Indian migrants in the present study has generally been reported in European populations, but there is also a report in Hong Kong Chinese.

In conclusion, body weight, serum cholesterol, and blood pressure are increased in Indians, who migrate to the UK. They already have higher serum Lp(a) than the indigenous population and this is unaffected by migration. Their insulin resistance is exposed as an increase in blood glucose and decrease in HDL cholesterol. On migration they acquire a CHD risk profile that is similar to that of the host community and which unmasks the underlying genetic risk of coronary heart disease conferred by high serum Lp(a) and a predisposition to increased insulin resistance. These findings should be helpful in designing public health strategies to reduce underlying CHD risk in Indians in the UK.

We are grateful to Dr C Gordon for carrying out the insulin assays, to Dr S Kumar for HOMA calculations, and to Mrs Hilary Prais and Mrs Barbara Haines for skilled technical assistance.

The data on serum Lp(a) concentrations on subjects of European descent (Europids) is used with the permission of the Oxfordshire Stroke Project and the Medical Research Council Epidemiology Unit in Wales.

References

**Social services case-management for long-term mental disorders: a randomised controlled trial**

**M Marshall, A Lockwood, D Gath**

**Summary**

Case management arose in the USA as a solution to the difficulties of providing community care to people with severe mental disorders. The basic principle of the approach is that a case manager takes responsibility for a client; arranges an assessment of need, a comprehensive service plan, delivery of suitable services, and monitoring and assessment of services delivered. The case-management approach has been widely accepted, to the extent that recent legislation has made case-management the cornerstone of community care in the UK.

We did a randomised controlled trial to evaluate a social services case-management team for people with long-term mental disorders. Subjects were referred from hostels for the homeless, night shelters, a general-practitioner clinic for the homeless, the Oxford City Council homelessness unit, and local voluntary-sector group homes. Of 103 subjects referred, 80 consented to be randomised to treatment or control groups. At 14-month follow-up, as assessed by standardised interviews, there were no significant differences between groups in number of needs, quality of life, employment status, quality of accommodation, social behaviour, or severity of psychiatric symptoms. In the case-management group there was a significant reduction in deviant behaviour on a standardised behaviour rating scale (REHAB) (mean=0.79; 95% CI 0.26-1.32).

It is unfortunate, in view of the limited effectiveness we have shown, that social services case-management was not evaluated in randomised controlled trials before its implementation in the UK.

*Lancet* 1995; **345**: 409-12

See Editorial page 399

**Introduction**

People with long-term mental disorders have many social and psychiatric needs.1 Since the closure of psychiatric hospitals in the UK, services required to meet these needs have become dispersed among different sites and providing authorities,2 with the consequence that many people with mental disorders are unable to obtain the care they need.3 In the USA, case-management arose as a solution to this problem of dispersion; this approach has been widely accepted4 and recently became the cornerstone of community care in the UK. Under the NHS and Community Care Act 1990,5-8 the responsibility for implementing case-management in the UK has been given to social services departments, who promote case-management teams to work with the mentally ill.4-6

In the UK, as elsewhere, the practice, composition, and organisation of case-management teams vary. Some UK teams work entirely within social services departments; others are jointly managed by social services and mental health services, or by mental health departments; others are jointly managed by social services and mental health services, or by mental health services alone.9 Nevertheless, teams share basic principles of the case-management approach: a case-manager, who takes responsibility for a client, arranges an assessment of need, a comprehensive service plan, delivery of suitable services, monitoring and assessment of services delivered, and also evaluates results.10,11 The expectation was that, by working alongside existing services, case-management teams would improve the quality and efficiency of care for patients with long-term mental disorders.12

The case-management approach has been described as “intuitively appealing”13,12 but there is little evidence that it is efficacious. The only randomised trial of an approach comparable to that practised by UK case-management teams was carried out in the USA and showed that the case-management group received more services than the control group and were more often admitted to mental hospitals, but showed no improvements in quality of life.12

---