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<th><strong>Title</strong></th>
<th>Responses of plasma concentrations of A type natriuretic peptide and B type natriuretic peptide to alacepril, an angiotensin-converting enzyme inhibitor, in patients with congestive heart failure [4]</th>
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<td><strong>Author(s)</strong></td>
<td>Cheung, B; Yoshimura, M</td>
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Insulin resistance, high prevalence of diabetes, and cardiovascular risk in immigrant Asians

Sir,—We read with interest the findings of Dhawan et al., who highlighted the importance of hyperinsulinemia, central obesity, and physical inactivity as risk factors in Asians with angiographically significant coronary artery disease. Both British and Indian Asians were found to share a predisposition to insulin resistance and its associated metabolic abnormalities—and hence a high cardiovascular risk. They conclude that this finding is likely to favour a genetic rather than an environmental basis for the recognized high mortality in this ethnic group. However, migrants are not a random sample of the original population, and their “selection” is likely to be determined by several health and socioeconomic factors, which are likely to influence their morbidity and mortality. If this environmental effect were a significant determinant of cardiovascular risk, one would not expect to see the high mortality from ischaemic heart disease (IHD) that has been recorded in Indians in South Africa,1 Trinidad,2 and Singapore,3 which emigrated over a century ago.

We recently reported a survey in which we studied the cardiovascular risk factor profile of all Asian men admitted with acute myocardial infarction during 8 weeks to our city centre district general hospital in Birmingham, England, and to the San Fernando General Hospital, in Trinidad.4 74 patients were studied (55 patients (mean (SEM) age 58.1 (1.4) in Trinidad (Trinidad group) and 19 in Birmingham (62.1 (2.6) (UK Group) (table)). We also found that mean systolic and diastolic blood pressures were higher in those with hypertension in the Trinidad group and 136-9 to 144 (11.4-8) mm Hg than in the UK group (120.8 (25.4)/75.0 (13.4) mm Hg, P < 0.05).5 Though Asians in Trinidad have in many ways adapted to the lifestyle of the host population, this does not appear to have reduced their cardiovascular risk profile, because those admitted with acute myocardial infarction had, in fact, a greater prevalence of central obesity, smoking, and higher blood pressures than a similar group from England.4

Central obesity and physical inactivity were common to both communities in England and Trinidad and their relation to insulin resistance may be particularly important in Asians with IHD. Our data support the hypothesis of a genetic predisposition to central obesity and diabetes in Asians that seems to have been retained by third generation Asian immigrants in Trinidad. This may explain the persistently high mortality from IHD in Asians.

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Quality of life in heart failure treated with enoximone

Sir,—The Enoximone Investigators concluded that in severe heart failure enoximone reduces survival but has a beneficial effect on the quality of life of survivors. As they indicate, if true, this is an important finding with interesting and difficult implications for drug regulatory bodies and for clinical practice. However, a statistical artefact could explain the result without there necessarily being any benefit from enoximone.

At randomisation, the two groups were reasonably well matched for measures of severity and demographics. As the trial progressed there was differential mortality between the groups. It is not unreasonable to assume that those who died had more severe disease and a worse quality of life than those who survived. Thus, even if there were no change at all in quality of life, the survivors will have a better average quality of life than the study group as a whole. Since more died in the enoximone group, this group will have lost more patients with poor quality of life, and enoximone will appear to have been beneficial.

Other evidence from the paper supports this interpretation of the results. Namely, the greater proportion of enoximone treated patients withdrawn from the trial and the greater proportion admitted to hospital. The improvement seen in the disease-specific measures after 2 weeks (when deaths were 8/8, from table 3) was probably genuine, but the lack of differences at three months and one year was unlikely to be because of lack of power alone (although 95% confidence intervals for the differences in means were not quoted). Indeed, as one would have expected the group with more deaths to have a better average quality of life for the reasons given, the possibility arises that quality of life actually diminished on enoximone treatment.

Apart from the baseline comparison, we are not able to interpret the Nottingham Health Profile (NHP) data at all. For example, the median physical mobility score in the enoximone group was 22 at one year, but there is nothing to compare this with. In many studies, we are not told what the median baseline score was; for example, in the enoximone group it would have been interesting to see the results on the other NHP dimensions.

There are ways round this problem, but none is fully satisfactory. We can assign all patients who died to the bottom half of the distribution of quality of life scores (for example, by giving them all the worst possible score). The median is then not biased for comparative purposes. However, if more than half the subjects for one median becomes uninterpretable (although in the Mann-Whitney U test remains valid).

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Responses of plasma concentrations of A type natriuretic peptide and B type natriuretic peptide to alacepril, an angiotensin-converting enzyme inhibitor, in patients with congestive heart failure

Sir,—Yoshimura and colleagues showed that the response of plasma brain natriuretic peptide (BNP) after 6 hours of atrial natriuretic peptide (ANP), and that the changes in pulmonary artery wedge pressure did not correlate with plasma BNP.1 This lack of correlation may be the result of this difference in responses.

We may be relevant to recall that BNP has a longer half life than ANP does and that the changes in pulmonary artery wedge pressure did not correlate with plasma BNP.1 In the present study, the slow half life of BNP may mean that there may also be a qualitative difference in the synthesis and release of BNP. In

Risk factor profile of men admitted to hospital with acute myocardial infarction in Trinidad and Birmingham

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<th>UK (%)</th>
<th>Trinidad (%)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Prevalence of Diabetes</td>
<td>32</td>
<td>36</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>32</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td>Smokers</td>
<td>42</td>
<td>91</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Regular alcohol use</td>
<td>21</td>
<td>11</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean waist to hip ratio (mean (SD))</td>
<td>0.95 (1.01)</td>
<td>1.01 (0.05)</td>
<td>&lt;0.001</td>
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rats, atrial stretch induces a rapid increase in BNP mRNA but not in ANP mRNA, although both peptides are released.1 The secretion of BNP seems to result from increased gene expression. This might explain the observation that intravenous saline loading raises plasma ANP but not plasma BNP within 60 minutes, but ingestion of salt tablets raises the plasma concentration of both peptides after 5 days.1 Indeed, the response of plasma BNP to saline loading is slower than the ANP response in patients with right ventricular failure (Morice AH, personal communication). Further studies of the relation between BNP and volume status may shed light on this important subject.

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This letter was shown to the author, who replies as follows:

Sir,—Plasma concentrations of ANP and BNP increase in patients with heart failure and correlate well with the degree of left ventricular dysfunction in patients with chronic heart failure. The relative concentrations of ANP and BNP both increase as the heart becomes overloaded. However, ANP concentrations increase before BNP concentrations.1 Plasma ANP increases mainly through secretion from vesicles that store ANP in the atria (regulated pathway). None of the less, BNP mRNA is expressed earlier than ANP mRNA.2 This is probably because ANP has the characteristics of an acute phase reactant whereas ANP mRNA does not.4 Clinical studies showed that BNP is secreted mainly from the ventricles in normal subjects and patients with mitral valve disease.5,6 Therefore, we disregarded the amount of BNP secreted by the atria, nearly all the circulating BNP originates from the ventricles.7

And my colleagues showed that the time courses of changes in plasma ANP and plasma BNP were different when cardiac overload was reduced by administration of an angiotensin-converting enzyme inhibitor.8 The mechanism is probably related to the different secretion sites and pathways of ANP and BNP: ANP is mainly secreted by a regulated pathway in the atria and BNP by a constitutive pathway in the ventricles. Other factors may also be involved in the mechanisms—for example, the direct action of angiotensin-converting enzyme inhibitor on the degradation of ANP and BNP. Thus the mechanism by which the changes in plasma ANP and BNP may be different when the cardiac load is increasing and decreasing. As Dr Cheung indicates, regulation of the natriuretic peptide system is important and complex. The mechanisms responsible for the changes in plasma ANP and BNP involve different patterns of synthesis, storage, secretion, and degradation.

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Transcatheter occlusion of cardiac defects

Sir,—Gatzoulis, Redington, and Rigby et al reported their experience with transcatheter occlusion of the ductus arteriosus and of atrial septal and ventricular septal defects with the Rashkind ductal umbrella device. We are somewhat surprised that they made no mention of the buttoned device that we and others used in transcatheter occlusion of the ducrtus arteriosus and atrial septal defects.9,10 We now have considerable experience with this device in nearly 400 patients with atrial septal defects, 120 patients with a patent ductus arteriosus (PDA), and eight patients with ventricular septal defects (unpublished observations).

Patent ductus arteriosus—Our experience with the buttoned device9 indicates that it has several advantages over the Rashkind device.9,10 We have included large tubular ducts with no obvious stenosis at the pulmonary end.1 All sizes and types of ductus11 can be successfully closed with the buttoned device, with at least 11F sheath sheaths, which had to be used in most of Gatzoulis’s patients. The success rate for device implantation was 86% for the Rashkind device and 97.5% for the buttoned device. Problems such as embolisation into the left pulmonary artery, inability to occlude the defect in a few patients, and severe haemolytic anaemia reported by Gatzoulis et al were not seen in our 120 patients. Residual shunts on colour flow mapping, particularly in infants who had 17 mm Rashkind umbrela devices implanted were higher in our patients than those that we saw with the buttoned device. Finally, there has been increasing concern about the development of stenosis of the left pulmonary artery after implantation of the Rashkind device especially in young children. Thus the buttoned device seems to have several advantages over the Rashkind device and it is hoped that, with further clinical trials, the buttoned device will prove to be useful in transcatheter occlusion of arterial ducts of all types and sizes.

Atrial septal defect—Redington and Rigby modified the buttoned device, created a reducer, and used it to close interatrial communications of various types. Of the 11 patients with fenestrated Fontan, there were two (18%) procedural failures. They were successful in closing defects, with only minor left-to-right shunts; the two remaining patients required surgical removal of the device and closure of the defect. In our more recently reported experience, which analysed the data of the first 180 patients,14 devices (7-7%) were dislodged. The dislodgement rate has improved with experience and with successive generations of the device. The third and second generation devices became dislodged in about 1% of patients. However, in the third generation device the dislodgement rate was 3-1% (2 of 65); this has further decreased to less than 1% in the fourth generation buttoned device (unpublished observations). Redington and Rigby placed a bend in the arm of the device. Such a bend is thought to be the reason why the arms of the Rashkind device broke off in our patients. The device was withdrawn from clinical trials.

Ventricular septal defect—Redington and Rigby concluded that their data do not support the routine use of a Rashkind PDA occluder to close patent ductus arteriosus or ventricular septal defects. We agree. Our own experience in occluding ventricular septal defect with buttoned device, though successful, is limited. Therefore, we cannot draw definitive conclusions on the superiority of the buttoned device.

In conclusion, the reports of Gatzoulis, Redington and Rigby et al showed the usefulness of the Rashkind PDA occluder in highly selected patient subgroups. We submit that the buttoned device has a greater utility in a wider range of patient subsects, although definite conclusions can only be drawn after longer clinical trials.

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