Contractile effect of sumatriptan in absence of U46619 (open circles, n = 4), and in presence of EC50 concentration (filled circles, n = 4). EC50 concentration (open triangles), or EC50 concentration (filled triangles) of U46619 on non-atherosclerotic epicardial coronary arteries.

Specimens were obtained from 4 patients aged 25, 29, 43, and 64 years, receiving heart transplantation for cardiomypathy. Experiments were done in duplicate in vessels from each patient. (Initial response U46619 concentrations shown by different starting points for each curve on the y axis.) M = mol/L.

The recommended dose of subcutaneously administered ergotamine is 10 to 48 times lower than for subcutaneous sumatriptan4 (table). However, the 100-fold higher potency, combined with the 2-fold higher maximum effect, as well as the much longer duration of action of ergotamine, suggests that, in general, the cardiac liability of ergotamine is higher than that of sumatriptan. Both drugs are contraindicated in patients with known coronary artery disease. Possibly, the oral administration of sumatriptan—if feasible—would lead to a less rapid rise in plasma concentrations, which could be safer in patients who may be at risk from coronary side-effects.


**Tumour HER2 protein in breast cancer and family history**

**SIR—**The HER2 gene, located on the long arm of chromosome 17, codes for a protein with the characteristics of a growth factor receptor.1 The ligand may belong to a family of proteins called heparin-binding growth factors.2 HER2 protein overexpression in breast cancers is associated with poor prognosis.3 Moreover, HER2 overexpression is positively correlated with inflammatory tumours, higher tumour mitotic activity, high tumour grade, large tumour size, and young age. HER2 overexpression is negatively correlated with tumour oestrogen and progesterone receptor content.4 We report that high tumour HER2 protein is also associated with a family history of breast cancer.

We measured HER2 protein in 20 women who had breast cancers excised in our centre, HER2 protein in the tumours was measured by enzyme-linked immunosorbent assay (ELISA), which, being quantitative, may be preferable to immunohistochemistry or western blotting, which are semiquantitative.5 All assays were done by Diacon Systems, Stratford, Connecticut.

HER2 concentrations were significantly higher in women with a family history of breast cancer (p = 0.0025, two-tailed Mann-Whitney U, figure). The 10 women with family history were predominantly post-menopausal (mean age 64.4 [SE 3.1] yr 57 [4.7] for the other 10; p not significantly different, t-test). There was no significant difference in tumour DNA index between the two groups (1.13 [0.08] vs 1.28 [0.12]). Of the 10 women with a family history of breast cancer, 4 had a first-degree relative with the disease (mother or sister); the other 6 had a second-degree relative with breast cancer (aunts, cousins, or a niece).

A familial breast-ovarian cancer gene, BRCA1, has been localised to the long arm of chromosome 17.7,8 This gene, associated with breast cancer in women under age 45, is not the HER2 gene.9 In addition, there is evidence implicating at least two genes on the short arm of chromosome 17 in breast cancer carcinogenesis.10

<table>
<thead>
<tr>
<th></th>
<th>EC50 (nmol/L)</th>
<th>Emax (%)</th>
<th>Recommended dose (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td>158 (33)</td>
<td>104 (9)</td>
<td>..</td>
</tr>
<tr>
<td>Ergotamine</td>
<td>4 (2)</td>
<td>43 (5)</td>
<td>0.125-0.55</td>
</tr>
<tr>
<td>Sumatriptan</td>
<td>631 (128)</td>
<td>22 (5)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Mean (SE) shown, n = 6-11, taubutaneous.

**REFERENCES**


**THE LANCET VOL 341: MAY 29, 1993**
In African countries, low birthweight is twice as common as in western populations. 15% or more of infants lie below the 5th centile of growth, as indicated by US National Children's Health Study reference standards—reaching 25–40% in preschool and schoolchildren. Nevertheless, these conditions seem to inhibit subsequent cardiovascular disease. In black South African adults, coronary heart disease (CHD) is absent in rural dwellers, and remains rare in urban dwellers, despite the facts that a quarter have raised cholesterol concentrations, over half the men smoke, and hypertension frequency is higher than in the white population. However, with the slight rise in socioeconomic status and its sequelae, the prevalence of diabetes, by contrast with its near absence in the past, is as high in elderly rural blacks as in whites. In both populations the poor and less poor are affected.

Historically, in western populations up to the turn of the century, most people were very poor. Undoubtedly, low birthweight and malnutrition diseases such as rickets were far more common than now. Yet until the 1920s CHD was very uncommon: in the UK it was regarded as "a rare disease in hospitals." Similarly, in the USA, when Paul Dudley White was young (in the 1920s), records at Massachusetts General Hospital did not reveal "more than a rare case of CHD" among poor people, although cases did occur among the well-to-do. We therefore suggest that adverse factors at birth and immediately after manifest their long-term pathogenicity, with respect to CHD and diabetes, principally in a westernised setting—higher energy high-fat diets, smoking practice, and diminished physical activity.

What can we do toward clarification? Unfortunately, no anthropometric data at infancy are available for middle-aged black adults. As second best, we are seeking to learn from individual black patients with CHD and diabetes to what extent their early family life was very poor, average, or better off.

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Fetal nutrition and cardiovascular disease in adult life

Sir,—Professor Barker and colleagues' findings (April 10, p 938) indicate that babies small at birth or during infancy have increased rates of cardiovascular disease and diabetes as adults.

Lying in juxtaposition with Africans, traditionally living and transmigrational, we are uncertain how much of their health/ill-health is regulated by genetic and environmental factors, dietary and non-dietary. African village children, equally poor and eating the same limited range of foodstufts, show wide ranges in various indices (anthropometrical, biochemical, haematological, faecal pH), which are not fully explained by carefully assessed dietary intakes. Doubtless, factors of genetic origin, of very early childhood experience, and of differing individual reactivity to environmental factors are in operation.