A transverse plane transoesophageal echocardiogram showing a protruding mass consistent with an atheromatous plaque in the middle part of the aortic arch. This was the only abnormality detected that could explain a recent cerebrovascular event.

events. However, their study was limited by the inclusion of patients with peripheral embolic events, by the lack of data on the size, morphology, and exact position of the atheromatous plaques and because they compared their cases with controls with cardiac disease. In addition, the sensitivity of the transoesophageal technique for aortic arch disease is unknown. Their data were, however, suggestive of a genuine association between the aortic arch lesions and cerebral embolism, although they do not demonstrate cause and effect. We recently performed transoesophageal echocardiography on a 57 year old man with no obvious cause of a stroke, in whom the only abnormality was a protruding plaque in the middle part of the arch (fig). However, such a gross abnormality was not seen in the patients reported in our recent study. We did see evidence of much less dramatic aortic arch atheroma in a few of these patients, but not in enough of them to convince us of its pathogenic relevance, and usually the patient had clinical or carotid ultrasound evidence of diffuse atheromatous disease. We have seen other patients with a peripheral embolic event who had clear evidence of protruding and mobile thrombotic plaques in the descending aorta. We agree with Tunick and Kronzon that these abnormalities would not be detected by precordial echocardiography and are worth seeking. We still, however, have no data on optimum treatment for such patients. Although Tunick *et al* have, somewhat radically, removed a protruding plaque in one patient,⁴ this treatment cannot be recommended for all such patients.

Transoesophageal echocardiography did show interesting abnormalities in these patients that cannot be detected by conventional precordial echocardiography. However, it may not be possible to demonstrate anything more than an association of certain abnormalities with clinical events. The accumulating data on the patency of the foramen ovale, spontaneous contrast echoes, and atheromatous aortic disease do suggest a possible pathogenic role for these features in embolic events. We should now use this technique to evaluate treatments that might reduce the recurrence rate of embolic events in these patients.

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- 1 Thompson T, Evans W. Paradoxical embolism. *Q J Med* 1930;23:135-50.
- 2 Tunick PA, Kronzon I. Protruding atherosclerotic plaque in the aortic arch of patients with systemic embolization: A new finding seen by transoesophageal echocardiography.

Am Heart J 1990;120:658-60.

- 3 Tunick PA, Perez JL, Kronzon I. Protruding atheromas in the thoracic aorta and systemic embolization. *Ann Intern Med* 1991;115:423-7.
- 4 Tunick PA, Culliford AT, Lamparello PJ, Kronzon I. Atheromatosis of the aortic arch as an occult source of multiple systemic emboli. *Ann Intern Med* 1991;114:391-2.

von Willebrand factor in plasma: a novel risk factor for recurrent myocardial infarction and death

SIR—Raised concentrations of von Willebrand factor antigen (vWFAg), a specific product of the endothelium reflect damage to the endothelium. Jansson *et al* (*British Heart Journal* 1991;66:351-5) reported that high concentrations of vWFAg are present in ischaemic heart disease and predict reinfarction and mortality in survivors of myocardial infarction. Among the 123 survivors entering their study there were 88 cases of hypertension, diabetes mellitus, and smoking. Furthermore, the mean cholesterol concentration was 7 mmol/l, indicating hypocholesterolaemia in an unspecified number of patients.

Jansson *et al* point out that increased concentrations of vWFAg are found in diabetes mellitus. In the absence of symptomatic vascular disease, however, hypertension, hypercholesterolaemia,¹ and smoking² also act independently to increase vWFAg. We therefore asked whether vWFAg would still be increased in ischaemic heart disease once these risk factors for atherosclerosis were considered.

We studied 41 non-diabetic patients (mean age 59) six weeks after myocardial infarction (proven by a raised creatine kinase over 130 units/l with retrosternal chest pain typical or electrocardiographic changes or both. Twenty one of them said that they were current smokers, or smoking at the time of infarction, or had stopped in the year before infarction. Symptom free age and sex matched controls who were normotensive and normolipaeamic were recruited from individuals attending hospital for endoscopy or repair of varicose veins. Resting systolic and diastolic blood pressures (SBP, DBP) were recorded, and blood was taken for routine measurement of cholesterol and vWFAg (by ELISA). For statistical analysis we used the Mann-Whitney and Spearman's methods on Minitab. Both cholesterol (mean (SD)) 6.3 (0.9) mmol/l, $p = 0.0001$ and vWFAg (130 (39) IU/dl, $p = 0.0004$) were higher in patients than in controls (5.2 (0.9) mmol/l and 104 (37) IU/dl respectively), confirming the work of Jansson *et al*. SBP and DBP were not increased in the patients with ischaemic heart disease but the values did correlate with vWFAg (SBP $r = 0.34$, $p = 0.033$; DBP $r = 0.59$, $p = 0.0001$). vWFAg did not correlate with cholesterol.

A subgroup of 20 patients (12 smokers) with ischaemic heart disease also had hypertension ($n = 10$, blood pressure > 140 and > 90 mm Hg) or a raised cholesterol concentration ($n = 10$, > 7 mmol/l) at re-examination six weeks after discharge from hospital. The remaining 21 patients (12 smokers) were free of these risks. When these two groups were compared we found that those with either of these risk factors had significantly raised blood pressure (136 (18)/84 (10) mm Hg) and cholesterol (6.8 (0.8) mmol/l). vWFAg was also higher (153 (35) IU/dl) than in the patients without these risks (107 (28),

vWFAg concentrations in survivors of myocardial infarction and in controls. Mean values are indicated by bars.

$p = 0.0002$), which in turn was not higher than in the symptom free controls (figure).

Although vWFAg is generally raised six weeks after myocardial infarction, in many cases this may be because of hypertension or hypercholesterolaemia or both. The presence or absence of smoking did not influence vWFAg concentrations in any group. We suggest that survivors of myocardial infarction without risk factors for atherosclerosis may have minimal evidence of damage to their vasculature. Conversely, in those with risk factors the endothelial insult is maintained and such patients may be at risk of further cardiac events. It would be instructive to learn whether Jansson *et al* could confirm this by performing multivariate analysis in the patients in their study.

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- 1 Blann AD, Miller JP, Waite M, McCollum CN. Endothelial cell injury in the risk factors of atherosclerosis. *Br J Surgery* 1992: (in press).
- 2 Blann AD. Increased circulating levels of von Willebrand factor antigen in smokers may be due to lipid peroxides. *Med Sci Res* 1991;19:535-6.

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

SIR—Blann *et al* report that in a case-control study they found higher concentrations of von Willebrand factor antigen (vWFAg) in survivors of myocardial infarction than in controls. Our study on survivors of myocardial infarction was prospective and showed that high concentrations of vWFAg predicted an increased risk of reinfarction and cardiovascular mortality in univariate Cox regression analysis.

In Blann *et al*'s study only the subgroup of subjects with myocardial infarction and hypertension or raised cholesterol (and not the subgroup without these risk factors) had higher concentrations of vWFAG than controls. In Table 4 in our paper (*British Heart Journal* 1991;66:351–5) the results of multivariate Cox regression analysis demonstrate that the association between high concentrations of vWFAG and reinfarction or cardiovascular death was independent of these and other risk factors.

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Thallium scans in syndrome X

SIR—In their interesting retrospective study, Tweddel *et al* (*British Heart Journal* 1992;68:48–50) identified 100 patients with typical angina and normal coronary arteriograms (syndrome X). Thallium defects were found in 98% of the patients leading the authors to conclude that microvascular angina is commoner than generally appreciated. However, this conclusion must be treated with some scepticism because of work-up bias which commonly undermines claims for the diagnostic value of non-invasive testing in studies of this type.¹ Thus we are told that it is the practice at the Royal Infirmary, Glasgow to use the thallium scan as a screening test to select patients for angiography. Preferential selection of patients on this basis itself ensures a high prevalence of abnormal scintigrams in the 10% of their patient population with normal coronary arteries. Only if selection for angiography were independent of the results of thallium imaging could firm conclusions be drawn about the role of microvascular angina in syndrome X.

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- 1 Kottler TS, Diamond GA. Exercise thallium-201 scintigraphy in the diagnosis and prognosis of coronary artery disease. *Ann Intern Med* 1990;113:684–702.

SIR—Connoisseurs of the circular argument will find few better examples than that recently presented by Tweddel *et al*. They contend that the finding of a high incidence (98%) of abnormal thallium scans in a retrospective study of patients with angina and normal coronary arteries is indicative of a high prevalence of microvascular disease. Unfortunately this contention is completely invalidated by their own admission that abnormal thallium scans were used for the selection of such patients for angiography in the first place. This being the case, it is surprising that the incidence of abnormal scans was not 100%.

The authors fail to document the number of patients seen with angina during the period under study who had normal thallium scans and as a consequence did not proceed to

angiography. Thus it is impossible to estimate a possible lower limit for the true incidence of abnormal scans in such patients.

The assertion that the scan abnormalities detected represent microvascular disturbances is entirely speculative. Very few such patients have true myocardial ischaemia (reflected by lactate production on stress testing).¹ Indeed, the inability to demonstrate a correlation between severity of the scan defect and limitation of exercise capacity seems to indicate their lack of functional significance. On the contrary, as only 30% of the study patients had abnormal exercise tests the primary conclusion from this study must be the poor positive predictive accuracy and specificity of abnormal thallium scans for detecting significant coronary artery disease where the exercise electrocardiogram is normal.

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- 1 Greenberg MA, Grose RM, Neuberger N, Silverman R, Strain JE, Cohen MV. Impaired coronary vasodilator responsiveness as a cause of lactate production during pacing-induced ischemia in patients with angina pectoris and normal coronary arteries. *J Am Coll Cardiol* 1987;9:743–51.

These letters were shown to the author, who replies as follows:

SIR—A more thorough reading of our paper would have shown that we were of course careful to emphasise that our unit's general practice of using positive thallium tests as a pre-catheterisation screening test inevitably determines that a very high proportion of our patients have positive thallium tests. Our study was not, did not intend to be, and could not have been an epidemiological study. It set out to provide a description of thallium test findings in an otherwise unselected group of patients presenting with typical effort angina and entirely normal coronary arteriograms. These patients with normal arteriograms represented about 10% of all those undergoing coronary arteriographic investigation in our unit, a proportion that is not grossly different from general experience where thallium is not used as a pre-screening test. Our finding that 98% of these patients showed abnormal thallium tests thus at least suggests—we claimed no more—that abnormal thallium tests are not uncommon in such patients and indeed might be found, by extrapolation, in some 5% of patients undergoing diagnostic coronary arteriography in other units unless our population is very peculiar. We were of course also careful to emphasise that an abnormal thallium does not necessarily imply reduced perfusion, or "microvascular angina" (one current word for the cardiologist's syndrome X in our continuing state of uncertainty) since it might also reflect abnormal potassium handling by the myocyte. Exercise tests and lactate production are recognised as having limited sensitivity in diagnosing ischaemia. Gold standards are hard to find in this arena.

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BOOK REVIEWS

Atrial fibrillation. J Rawles. (Pp243; £49.50) Berlin, Heidelberg, New York: Springer-Verlag, 1992. ISBN3-540-19699-4.

Atrial fibrillation is the commonest of all chronic sustained arrhythmias and until recently there was little to add to the early descriptions. The past decade has seen significant advances, with confirmation of the circus movement hypothesis. The other major development is in the understanding of how the atrioventricular node influences the ventricular response. Simple conduction of a proportion of the impulses from the fibrillating atria has been disputed by others in the past, and Rawles now adds his voice and (very usefully) his mathematical model to explain the behaviour of the atrioventricular node as an oscillator. Is this all too abstruse and too basic for the practising clinician? By no means: this slim volume deserves the attention of all cardiologists.

This is the work of one author. Some of the mathematical aspects are difficult, but they are worth studying and you will see that the explanations are quite clear. From them, phenomena such as concealed conduction and therapeutic regularisation of the ventricular rate are now easier to understand in logical terms.

The author's own interest in the changes in the cardiac output that occur during atrial fibrillation are carefully explained, on the basis of the use of non-invasive measurements and with the promise of further and better understanding with the continued use of Doppler techniques. The causes, ways of presentation, and treatment are all discussed, but more in terms of understanding than as a "cook book" list. What is particularly helpful is the bibliography. This is not just an accumulation of references haphazardly collected but rather a set of articles cited at the end of each chapter, each one having precise relevance to statements made in the text. This alone makes the book an important contribution.

While the clinical section is comprehensive it is rather tightly written. Why do coronary artery disease and myocardial infarction each have a subsection, yet lone atrial fibrillation and the sick sinus syndrome do not? The omission of any mention of the syndrome of alternating bradycardia and tachycardia is a surprise in a book written in Aberdeen. The role of chronic bronchitis, previously commonly believed to be important, also deserves more attention and a section of its own.

The discussion on drug actions is relevant with understandably considerable emphasis on what is known about the way in which digitalis works. Others will have to do more work on the mode of action of calcium antagonists before the author can give them corresponding depth of treatment, but what he says about each group of agents is ample and appropriate. He mentions also the use of techniques of ablation and considers carefully the need for prevention of embolic stroke and the ways in which this can be done.

John Rawles has provided us with an extremely useful addition to our knowledge, and his book on atrial fibrillation is one that I