We studied 34 patients in sinus rhythm during dipyridamole stress and compared age matched coronary disease patients who developed ischaemia, detected by echocardiographic and electrocardiographic criteria, with those who did not.1 Transmirtal flow was uninterpretable in three (9%) patients owing to fusion of the early and atrial waves. Doppler filling variables were insensitive in identifying patients with ischaemia induction even when this was severe. Our data strongly suggested that changes in ventricular loading and heart rate induced by dipyridamole masked the expected effects of myocardial ischaemia on the filling profile. Other workers have reached similar conclusions indicating that this approach cannot supplement wall motion analysis for the evaluation of patients with coronary artery disease. Despite reservations on interpretability, the data from Shahi et al are consistent with these observations and highlight the ease with which spurious differences between groups may emerge when numerous confounding variables are operative and group size is small.  

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CELIA M OAKLEY
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This letter was shown to the authors, who reply as follows:

Sir—Dr Mazeika and Dr Oakley have quite rightly brought to the attention the differences in age between the control and study group which may have had an effect on our results. Both age and heart rate are well known to be important determinants of transmirtal Doppler filling velocities and as yet no correction factors are known to allow for these variables. Neither is it known how heart rate affects subjects of different ages or how heart rate affects patients with ischaemia and normal filling velocities in different age groups. Despite these unknown variables we feel that useful information can be derived from studying filling velocities during myocardial ischaemia.

All patients studied were in sinus rhythm both before and during the study period. Aminophylline was given to two patients in group 3A and one patient in group 3B. In two of these patients it was given at the end of the study period and therefore would not have affected the filling velocities.

Two patients in the control group developed a single filling velocity profile during the study period but only for a maximum of two readings. In these patients the filling velocity of the early filling wave just before merging of the waves was taken to represent the filling velocity.

To allow for baseline temporal variability the mean value of five one minute recordings was taken to represent baseline value.

Regional wall motion abnormalities were not specifically assessed in our study but their importance as a more sensitive marker of ischaemia was discussed in the discussion section (p 270).

Reference 5 quoted by Dr Mazeika and Dr Oakley was cited in our paper together with its limitations. We cannot comment on reference 4 at present.

Although it was not possible for technical reasons to assess the presence of mitral regurgitation during myocardial ischaemia in our study, Dr Mazeika and Dr Oakley are correct to state that this may have affected our results. Ischaemia-induced mitral regurgitation would increase left atrial pressure and therefore decrease the isovolumic relaxation period and subsequently increase the transmirtal pressure gradient with a resulting increase in the early filling velocity and a possible decrease in the atrial filling velocity. It is therefore possible that this may be the reason for the difference in left ventricular filling velocities in groups 3A and 3B. Both at the end of the abstract and in the discussion section we stated that our observations could be attributable either to the degree of myocardial ischaemia or to different haemodynamic changes occurring during myocardial ischaemia.

Once again we would like to emphasise that the study was designed to observe the left ventricular filling characteristics during myocardial ischaemia and not to suggest that these changes in filling velocities could predict myocardial ischaemia in an individual patient (last paragraph p 269).

I hope these comments will help clarify the points made by Dr Mazeika and Dr Oakley.

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Circadian variation in the frequency of onset of chest pain in acute myocardial infarction

Sir—Dr Thompson and colleagues make a convincing case in Leicester for a midnight peak in onset of myocardial infarction in addition to the well-known one at 8 am (British Heart Journal; 1991;66:177-8). They try to persuade us that meta-analysis of other studies would confirm this. Unfortunately they have omitted from their references perhaps the largest study of all. This was the collected data from the World Health Organis- 

ation Regional Office for Europe Heart Attack Registers of the 1970s covering some 10,000 events. The pooled data from these shows a clear peak between 8 and 10 am on weekdays which is much sharper at 10 am on Saturdays and Sundays. There is also a bulge around 4-5 pm but no overall peak around midnight. The exception interestingly is a possible such peak on Saturday. If the Leicester peak is not just a chance finding, and it is found in some cities but not others and may be related to Saturdays, one
wonders whether it is related to closing time in public bars.

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This letter was shown to the authors, who reply as follows:

STIR.—We thank Professor Tunstall-Pedoe for his interesting comments on our paper. The confirmation of the finding of a secondary midnight peak in the onset of chest pain in acute myocardial infarction in a five year retrospective analysis of a five year prospective study makes it unlikely that the peak is a chance finding. Our discussion reaches no conclusion about its possible cause but our data do not exclude the possibility that the midnight peak is a local phenomenon whose explanation might lie in local circumstances. We find the explanation in terms of public house closing times intriguing but unlikely to be correct. Our data, which have also been analysed for the frequency of acute myocardial infarction on days of the week (unpublished), do not provide significant support for the Saturday hypothesis. Moreover, a change of licensing hours applied to Leicester which liberalised weekday public house opening, occurred during the prospective data collection and did not result in a measurably stronger trend in support of the midnight peak during the later stages of the study.

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Syndrome X and hyperventilation

STIR.—Syndrome X and hyperventilation have long been associated, and Lewis and colleagues (British Heart Journal 1991; 165:94-96) are to be congratulated for their discriminating contribution to the field and for raising several important questions. A central issue is whether hyperventilation can be dismissed on the basis of a rather limited schedule of testing. For example, it is no longer thought that the forced hyperventilation provocation test (FHPVT) is the “gold standard” of hyperventilation testing, but that provocation by personally relevant stresses is at least as important. Indeed, in the context of cardiac patients, the latter stresses, which can also activate the sympathetic nervous system (with consequences such as magnesium depletion) it seems likely that it is the neuroendocrine setting that can determine whether or not a given episode of hyperventilation has vasocconstrictive consequences.

It is a commonplace finding that many patients with recurrent hyperventilation illnesses do not hyperventilate during an exercise test, but readily overbreath in response to an emotional challenge, particularly when the challenge involves the recall of feelings of being trapped or of anger.

As far as the data presented by Lewis et al are concerned, besides noting the absence of figures for end tidal pressure of carbon dioxide (C O₂) for their controls, we also note that the C O₂ values of 38 mm Hg at 50% of maximum exercise and 37 mm Hg at maximum exercise are well below expected normal values.

The demonstration of increased minute ventilation for given minute carbon dioxide (VE/VCO₂) is quite consistent with chronic hyperventilation. It is due either to reduced respiratory centre buffering or to a flywheel effect which regularly over-activated pathways promote breathing, or both. The observation of a raised VE/VCO₂ may well be the key indicator of a longer term tendency to hyperventilation, because as stated above, the FHPVT is a single act of hyperventilation and is dependent upon the patient’s starting point in terms of other influences upon vasoconstrictor activity, arterial hypotension and depletion of the body’s buffering systems.

A basic question about syndrome X patients is whether their responsiveness to recognised vasocconstrictive influences is greater than average, just as Europeans in general are more responsive than the Japanese.

We suggest that Lewis et al have sharpened the definition of characters in the drama of syndrome X and hyperventilation but have not yet brought down the final curtain.

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This letter was shown to the authors, who reply as follows:

STIR.—We appreciate the interest shown by Dr Nixon and colleagues in our paper. Our study refers of course to carefully characterised patients—an important consideration given the widely differing patient groups represented in published reports on patients with unexplained chest pain. Clearly the filing category of syndrome X is coming to the end of its useful life, particularly in view of the confusion now arising over a different “syndrome X”.

STIR.—We agree on the points raised by Dr Nixon and colleagues—our patients with syndrome X all described typical angina and, in every case, exercise induced the same symptom. We would argue that an exercise test in such a group represents a “personally relevant stressor”. The finding of normal arterial P CO₂ values during exercise in our syndrome X patients formed the basis for our conclusion that our patients were hyperventilating inappropriately (which in common usage is the implication inherent in the term). Because we showed that end tidal P CO₂ correlated only poorly with arterial P CO₂ in these patients, their end tidal measurements, we agree, provided no evidence either for or against a diagnosis of hyperventilation. Chronic hyperventilation may indeed increase the VE/VCO₂ slope but only in the presence of low arterial P CO₂ (the modified alveolar gas equation states: VE = 863 V CO₂/paco₂ (1 - VD/Vt)). The normal arterial P CO₂ in our patients may have increased in deadspace ventilation. We did not measure arterial P CO₂ in our control patients for ethical reasons.

We agree that the final curtain is not yet drawn on the various players on this ill-lit stage, while our spotlight continue to weave...
Circadian variation in the frequency of onset of chest pain in acute myocardial infarction.

H Tunstall-Pedoe

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