whether other branches of complementary medicine should be authorised.

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Single dose of oral dexamethasone for outpatient croup

Failure to follow up all patients is a concern

EDITOR,—G C Geelhoed and colleagues conclude from their study that oral dexamethasone at a dose of 0.15 mg/kg is effective in reducing return to medical care in children with mild croup.¹ The sample size seems adequate, though on the borderline for detecting a 90% reduction, but the fact that four children were not followed up is of concern. If the two children lost to follow up in the treatment group had in fact sought some medical care (or even died) this would have meant that the difference in outcome between the two groups was not significant by Fisher's exact test. We wonder why the calculation of sample size assumed such a large reduction as 90%. Was this a retrospective calculation?

The final key message states that all children presenting with croup should be considered for steroids. Before the authors' findings can be generalised we need to know what proportion of children who presented with mild croup were excluded from the trial and what the rate of parental refusal was.

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Authors should have stated how drug was given

EDITOR,—The results of G C Geelhoed and colleagues' trial of a single dose of oral dexamethasone for outpatient croup would be easier to apply in practice if we knew how the authors gave the dexamethasone.¹ Did they use the 500 µg tablets or a solution, and did they round the dose to the nearest 250 or 500 µg? Was the dose given in the emergency department immediately on diagnosis, or did a parent give it later after getting it dispensed?

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Authors' reply

EDITOR,—Rosie Helowicz and Jill Walton express concern about the children who were lost to fol-

low up in our study. Our follow up rate of 96% is extremely good when compared with follow up rates in other clinical studies of outpatient treatment. Although we could not follow up four children directly, we were able to ascertain that none of them presented to any hospital in the Perth metropolitan area in the 10 days after their original episode of croup.

Helowicz and Walton also point out that if the two children lost to follow up in the treatment group had relapsed then the results would no longer be significant ($P = 0.08$ by our calculations). On the basis of the outcome in the 96 other children in the study, however, it seems more logical to assume that the two children lost to follow up in the treatment group would not have relapsed, which would give $P = 0.003$. Rather than indulge in more "what if" scenarios, we think it worth noting that we saw 935 children with croup in our emergency department in the first six months of 1996, when it was standard practice to offer these children a dose of oral dexamethasone. Of the 668 children who were sent home, only 19 (2.8%) reattended, which is a much smaller proportion than the 15% we would have expected. In answer to Andrew Herxheimer's questions, children in the study were given a solution of oral dexamethasone BP (manufactured in our hospital pharmacy¹) in the hospital emergency department. The dose given was exactly 0.15 mg/kg.

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QTc dispersion and risk of cardiac death in peripheral vascular disease

Dispersion of 60 ms^{1/2} is insufficient to change clinical management

EDITOR,—Dawood Darbar and colleagues investigated the usefulness of QTc dispersion as a predictor of cardiac death in patients with peripheral vascular disease.¹ They compared QTc dispersion in a routine electrocardiogram in patients with peripheral vascular disease who had probably died of cardiac causes with that in those who survived. The mean QTc dispersion in these patients was 86.3 ms^{1/2} and 56.5 ms^{1/2} respectively. The authors claim that a QTc dispersion of 60 ms^{1/2} is highly predictive of sudden cardiac death. However, QTc is a continuous variable, so the normal distributions of the data for each group would be as shown in figure 1.

Although the figure of 60 ms^{1/2} is significant, in reality only patients with a QTc dispersion of >86 ms^{1/2} may confidently be considered to be at increased risk. Given that the mean QTc dispersion of the survivors was 56.5 ms^{1/2} with a standard deviation of 25.4, it is difficult to see how, in clinical practice, a QTc dispersion of 60 ms^{1/2} would be sufficient to alter the management of the patient.

There are also methodological problems with this qualitative measurement of QT dispersion. For example, estimating the end of the T wave as being at the nadir between a T and U wave² may lead to an underestimate. Determining the adjusted QTc dispersion by dividing the QTc dispersion by the square root of the number of

Fig 1—Diagrammatic representation of data of Darwood and colleagues¹

leads measured³ may compound qualitative errors that might be expected to arise from a high interobserver variability in QT measurement.

Although promising, the evaluation of dispersion of repolarisation from surface electrocardiography requires validation and would be much more useful clinically if qualitative bias could be removed. It is at present rather optimistic for QT dispersion to be considered the "electrophysiological Holy Grail."¹

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Three facets of the study need attention

EDITOR,—Darwood Darbar and colleagues showed the predictive value of QTc dispersion (≥ 60 ms) in patients with peripheral vascular disease,¹ but we think that three parts of this paper need attention.

The first is the patient population. This small, retrospective study was not controlled for risk factors, which introduces significant selection bias. Patients with peripheral arterial disease have a higher incidence of coronary artery disease and its complications. Ischaemic burden (symptomatic or asymptomatic) and the severity of coronary stenosis influences prognosis.² Mean ejection fraction is useful, but in individual patients the above events clearly alter the prognosis, with only a small change in mean ejection fraction. The paper fails to correct for these influences. Several earlier studies have found QTc not to be a predictor of ventricular tachycardia or ventricular fibrillation even in patients after a myocardial infarction.³ Therefore, we wonder whether this test would still be predictive in a multivariate analysis.

The second is that the measurement of QT and QTc dispersion is unstandardised⁴ and shows wide variability even with digitised boards.⁴ Darbar and colleagues do not mention the exact method of measurement, but the impression is that it was manual. With three observers measuring QTc, we find it surprising that interobserver or intraobserver variability was not evaluated. Why do the authors cite studies observing large errors in QT dispersion assess-

ment when they surely must have their own variability data? The claim that the differences seen in this study were greater than the variability published earlier gives the impression that readers are asked to accept apples and oranges as identical.

The third is relevance. The study reports values of QTc dispersion without QT duration, QT dispersion, and heart rate. Despite some probably appropriate criticism, Bazett's formula indicates that the duration of the QT interval depends on the heart rate. However, we fail to see why QT dispersion should depend not only on heart rate but also on the duration of QT interval in the same mathematical way. Heart rate itself is an important prognostic indicator in coronary artery disease.⁵ If the authors were dealing only with measurement inaccuracy and effectively measuring not QTc dispersion but a random error (identical in all patients), the same results would still be achievable because in patients with faster heart rate this measurement error would be "corrected" into a higher "QTc dispersion." In other words, reporting QTc duration and dispersion without mentioning QT interval and dispersion and heart rate is as insufficient as reporting training induced changes in exercise capacity without describing subjects' physical state and age.

To summarise, the use of QTc dispersion in inappropriate situations makes the potential utility of this measure more complicated, especially if accepted prognostic indicators and serious technical problems and problems with data analysis are ignored.

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QTc dispersion and vulnerability to ventricular fibrillation

EDITOR,—Dawood Darbar and colleagues report that QTc dispersion has a high degree of sensitivity and specificity for predicting cardiac death in patients with peripheral vascular disease.¹ In the accompanying commentary R Campbell expresses concern that, although it is an extremely useful non-invasive marker to identify patients at increased risk of cardiac death, protective strategies are extremely limited.¹

Ischaemic preconditioning is one of the most powerful protective mechanisms in human myocardium.² Recent reports suggest that preinfarction angina improves in-hospital mortality and the electrical stability of myocardium through the induction of ischaemic preconditioning.³ We therefore investigated the

association between acute myocardial infarction and QTc dispersion in 35 patients with or without preinfarction angina. All patients were admitted within six hours of the onset of symptoms and underwent coronary angiography 90 minutes after intravenous thrombolysis. Preinfarction angina was defined as new onset or worsening angina seven or less days before acute myocardial infarction. QTc dispersion was calculated from 12 lead electrocardiography on hospital admission and 24 hours later. Heparin treatment resulting in an activated partial thromboplastin time between two and three times the control value was continued for 24 hours. Preinfarction angina was reported in 16 patients.

Age, sex, delay in treatment, reperfusion time, and patency of the infarction related coronary artery at 90 minutes was similar in patients with or without preinfarction angina. However, QTc dispersion was less in the electrocardiogram on admission in patients with preinfarction angina (43 (15) ms) than in those with no preinfarction angina (77.3 (20) ms, $P = 0.001$). At 24 hours, this trend persisted between the two groups (62 (22) ms v 71 (22) ms, $P = \text{NS}$). The results show preinfarction angina is associated with reduced QTc dispersion, and this protection may be conferred by ischaemic preconditioning. Furthermore, ischaemic preconditioning has also been shown to reduce the incidence of ventricular arrhythmia in patients with acute myocardial infarction.³

As pointed out by Darbar and colleagues,¹ these studies show that strategies to reduce QTc dispersion and improve electrical stability of the myocardium are possible. In future, we may be able to use preconditioning mimetic agents to improve patient prognosis.⁴

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QTc dispersion also occurs in diabetes

EDITOR,—Dawood Darbar and colleagues showed a strong link between QTc dispersion and cardiac death in patients with peripheral vascular disease.¹ Their results have great importance because the risk of sudden unexpected death could easily be evaluated by a simple and non-invasive method. QTc dispersion was associated mostly with diffuse coronary disease, suggesting that myocardial fibrosis could be one of the most important causes of electrical heterogeneity leading to fatal arrhythmias. Chronic heart failure, ischaemic heart disease, and hypertrophic cardiomyopathy resulting in QTc dispersion might have a similar mechanism. I should like to add a further clinical condition to the list which perhaps has a different explanation for the QTc dispersion.

Cardiac autonomic neuropathy is a well recognised specific complication of diabetes mellitus. The clinical consequences of autonomic neuropathy include prolongation of the QT

interval in diabetic patients.^{2,3} It has been suggested that sympathovagal imbalance due to cardiac autonomic neuropathy might have resulted in prolongation of the QT interval in these patients. QT dispersion was also observed in diabetic patients,⁴ and QT interval dispersion was an important predictor of mortality in patients with non-insulin dependent diabetes in a recent prospective study.⁵ Regardless of the exact mechanism, measurement of QT dispersion could be a cheap but valuable tool for detecting patients at risk of sudden cardiac death, including diabetic patients with cardiac autonomic neuropathy.

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Authors' reply

EDITOR,—We agree with Nicholas J Linker and Adam P Fitzpatrick that a QTc dispersion of 60 ms^{1/2} would be insufficient in clinical practice to alter the management of a patient with peripheral vascular disease. However, we chose this cut off point because it had optimal sensitivity and specificity in predicting cardiac death and was based on the receiver operating characteristic curve. All cut off points are artificial to some extent and highly dependent on the population studied. The risk of cardiac death is likely to increase as QTc dispersion increases, but our study was too small to show this. Clearly, a QTc dispersion of >100 ms^{1/2} is much more meaningful in clinical practice and should alert a clinician to consider investigations and treatments in a patient. One further point that should be noted is that the QTc dispersion in the survivors (56.5 (25.4) ms^{1/2}) was in the same range as that established for healthy subjects in the study by Sylven et al (54 (27) ms^{1/2}).¹ In contrast, patients who died of probable cardiac causes showed a substantially greater and significant increase in QTc dispersion (86.3 (23.9) ms^{1/2}).

As Krishna Prasad and colleagues point out, the severity of coronary artery stenosis in patients with peripheral vascular disease influences prognosis. The crucial point is that coronary angiography, which is required to determine coronary anatomy is invasive and not applicable to all such patients. In contrast, QT dispersion is an easily obtained, non-invasive test that may be widely applicable. Nowhere do we claim that QT dispersion is the most accurate test, but it could be the easiest to apply in large populations of patients. In addition, as table 3 shows, there was a non-significant trend towards increased QTc dispersion with increasing severity of coronary stenosis. The mean ejection fraction showed no such association. As for other risk factors, hypercholesterolaemia and smoking were more common in the survivors while hypertension and diabetes were more prevalent in those dying of cardiac causes. QT dispersion and heart rate were not reported due to limitation of space; QT dispersion was significantly prolonged