analysed blood samples of men taken when they entered the study—so that these included both the survivors and non-survivors of myocardial infarction. This is an important and essential feature not included in the other studies. The results showed no association between the D allele and the risk of ischaemic heart disease or myocardial infarction. The odds ratio for risk of ischaemic heart disease in the overall group of patients with the DD genotype compared to the other two genotypes (ID and II) was 1.09 (95% confidence interval 0.92 to 1.27), and for myocardial infarction was 1.08 (95% confidence interval 0.85 to 1.38). These negative results could be due to the heterogeneous genetic background of this North American population, which may have been too diverse to show an association between ACE gene polymorphism and ischaemic heart disease. Other reasons could be suggested, such as that the men in this study may have been at too low overall risk. Possibly, however, there may simply be no association.

Nevertheless, the renin-angiotensin system has a crucial role in the pathogenesis of ischaemic heart disease. This is shown by the undoubted benefits of angiotensin converting enzyme inhibition in reducing ischaemic events^{10 11} and the evidence from many laboratory and clinical studies. This clinical benefit is thought to be due either to reduced formation of angiotensin II as a result of angiotensin converting enzyme inhibition or to variations in types or responses in angiotensin II receptors. Further work from Cambien's group has suggested other reasons for the increased risk of coronary artery disease—such as a synergistic effect of the increased levels of angiotensin converting enzyme associated with the D allele and a polymorphism of the gene for the AT1 receptor (a subtype of angiotensin II receptors)¹²; or another polymorphism in the ACE gene which influences the plasma concentrations of angiotensin converting enzyme—which in turn may be an independent risk factor for myocardial infarction.¹³ Yet other studies have suggested that a variant of the angiotensinogen gene (T235) may play a part.¹⁴ This last genetic variant is also associated with essential hypertension in both white¹⁵ and Japanese populations¹⁶ and may potentially be concerned in several pathways leading to the pathogenesis of ischaemic heart disease.

Where do we stand? The early promise that the ACE I/D gene polymorphism would prove to be an independent risk factor for ischaemic heart disease has not been substantiated by other studies. The interaction of angiotensin

converting enzyme and the renin-angiotensin system has, however, important actions on blood vessels, including modulation of the formation of the atherosclerotic plaque. At present the responsible genetic factor has not been identified, but one or more genetic risk factors or markers from the angiotensin converting enzyme renin-angiotensin systems may well be found. The genetic basis for ischaemic heart disease has always been assumed to be multifactorial.

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Postoperative shivering: the influence of body temperature

May be related more to peripheral than core temperature and can be reduced by space blankets

Postoperative shivering is common.¹ During recovery from anaesthesia increased muscular activity increases oxygen consumption as much as fivefold. Hypoxaemia, lactic acidosis, and hypercarbia may then complicate recovery from anaesthesia,² at a time when the patient is at risk of hypoxaemia from other causes. Even without these complications patients find shivering uncomfortable, and preventing the syndrome is clearly desirable.

Why do patients shiver postoperatively? It is tempting to assume that heat loss is contributory, exacerbated by peripheral vasodilatation that in turn is induced by volatile anaesthetic agents. Normal thermogenic shivering is initiated by the hypothalamus. Temperature receptors in the skin, viscera, and various levels of the neuraxis provide information

on temperature which is processed at multiple levels of the spinal cord and brain before reaching the hypothalamus. Afferent information on temperature from the head and neck reaches the hypothalamus through the trigeminal nucleus.^{3 4}

Although core hypothermia is not a prerequisite for postoperative shivering,¹ manipulation of thermal inputs may influence the expression of postoperative shivering. For example, applying radiant heat to the face or chest may abolish postoperative shivering without affecting core temperature.⁵⁻⁷ Buggy and Hughes conducted a randomised controlled study of pre-emptive protection with a space blanket.⁸ Five (15%) patients wrapped in a blanket before induction of anaesthesia shivered postoperatively, compared with 21 (63%) controls. Core temperatures did not differ

significantly throughout the study, although peripheral temperature increased progressively in both groups. This increase was significant in those protected by the space blanket. In recent studies of intraoperative heat balance there was a relation between peripheral temperature and postoperative shivering but not between core temperature and shivering.⁹

Anticholinergic drugs increase postoperative shivering by a peripheral mechanism,¹⁰ which may be due to peripheral vasodilatation and consequent loss of heat from the skin. In women, postoperative shivering is more common during the luteal phase of the menstrual cycle than during the follicular phase, an effect that may be due to the vasodilatory effects of progesterone.¹¹ The importance of the study by Buggy and Hughes is that it emphasises the importance of afferent information on temperature from areas other than the core in the aetiology of postoperative shivering.⁸ The aetiology is clearly multifactorial, the factors including the patient's age and sex and aspects of the anaesthetic technique such as premedication, the identity of the induction agent, and the ventilatory technique used.¹²

Although Buggy and Hughes's study suggests that preventing the syndrome may not be difficult, current management emphasises treatment. Firstly, measurement of the core temperature is important as hypothermia must be treated concurrently with shivering to prevent further cooling. Drugs

remain the most popular mode of treatment. Intravenous pethidine (0.3 mg/kg) will abolish shivering in most subjects. Doxapram (1.5 mg/kg) is also effective.¹ My preference is for pethidine as it is effective in small doses without major side effects and contributes to some extent to postoperative analgesia.

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Managing cleft lip and palate

Continental Europe may do it better than Britain

The management of cleft lips and palates, owing to their complex and protean nature, is often unsatisfactory. Worryingly, the two British centres in a recent study of six European centres had the worst results.¹ A Medline search shows that over the past two years 25 publications have reported the results of cleft surgery: 16 from continental Europe, four from the United States, two from other countries, and one from Britain. This year's July/August issue of the German maxillofacial journal, *Deutsche Zeitschrift für Mund-Kiefer und Gesichtschirurgie*, is almost entirely devoted to cleft lip and palate surgery. Why are British results poor and British studies of outcome conspicuous by their absence?

Continental Europe seems to have a different approach to cleft surgery. One important difference is anatomical specialisation. Although this is usual in most other British surgical specialties, cleft surgery has often remained one part of a broad surgical practice. In most centres in continental Europe cleft lips and palates are managed by surgeons specialising and practising mainly in the maxillofacial region. Cleft surgery therefore becomes one of many maxillofacial procedures, and the surgeon is a "high volume" operator in this complex anatomical area. Compare this with a more general approach, where the surgeon may stray into the maxillofacial area only occasionally. In Britain "high volume" maxillofacial surgery exists at district general hospital level. Using surgical protocols and multicentre studies provides a well tried method of collecting enough cases to audit outcomes.²

After the Eurocleft study¹ a report of current surgical activity in England and Wales found that few surgeons had the caseload of primary repairs thought to be desirable by an expert working group.³ The authors of a report on current activity argued for the centralisation of services on regional multidisciplinary teams,⁴ and these recommendations have

now been published.⁵ Yet large units, with single surgeons undertaking adequate numbers of cases, do not guarantee good results—as experience in Britain has shown over the past 50 years. And treating patients in large, sometimes remote, centralised units has other problems. There may be difficulties in fully informing and involving all the local support teams, not least the local paediatric services. Should patients travel considerable distances to get, for example, speech therapy when local district general hospitals are well placed and funded to provide such a comprehensive service?

Excellent results require excellent primary surgical techniques, and surgeons in Britain may have something to learn from their colleagues in continental Europe—for example, functional surgery. This technique, which carefully restores the anatomy damaged by the clefting, results in better function and more normal growth and development.^{6,7} Although studies comparing this technique with those commonly used in Britain suggest that functional surgery produces consistently better results,⁸⁻¹¹ only about a fifth of patients with cleft lip and palate in Britain are treated this way.¹² Surgeons in Britain should look across the Channel at both the training of cleft surgeons and surgical techniques—their patients have much to gain.

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