CORRESPONDENCE

Because we receive many more letters than we have room to publish we may shorten those that we do publish to allow readers as wide a selection as possible. In particular, when we receive several letters on the same topic we reserve the right to abridge individual letters. Our usual policy is to reserve our correspondence columns for letters commenting on issues discussed recently (within six weeks) in the BMJ.

Letters critical of a paper may be sent to the authors of the paper so that their reply may appear in the same issue. We may also forward letters that we decide not to publish to the authors of the paper on which they comment.

Letters should not exceed 400 words and should be typed double spaced and signed by all authors, who should include their main degree.

British blood cholesterol values and the American consensus

SIR,—Attention has recently been drawn to the NIH consensus development conference statement on lowering blood cholesterol values to prevent heart disease (11 May, p 1493). The full statement has now been published[1] with a supporting editorial. Few would object to the editorial advice to stay close to the ideal weight,[2] not to smoke, and to take reasonable exercise, though there might be some argument about what constitutes a "healthy heart diet." However, the detailed consensus statement includes specific recommendations about screening for blood cholesterol values and taking appropriate action. These need to be critically reviewed in a British context.

The consensus panel concluded that individuals with high risk blood cholesterol values (above the 90th centile) should be treated intensively by diet, and if response to diet was inadequate appropriate drugs should be added. Adults with moderate risk values (between 75th and 90th centiles) should be treated intensively by diet; only a small proportion would require drug treatment. In subjects of 40 years and over high risk is defined as >6·72 mmol/l (259 mg/100 ml) and moderate risk as >6·21 mmol/l (240 mg/100 ml).

What do these recommendations mean for the British population? There is good evidence that British men have higher blood cholesterol concentrations than American men, and comparison of the distributions in British and American men provides a disturbing view of the effect of applying American derived centiles to the British blood cholesterol concentrations.

The American data are derived from the Lipid Research Clinics programme[3] and include 8483 white men aged 40-59 years drawn from 10 centres during 1972-5. The 7735 British men aged 40-59 years were randomly selected from the age-sex registers of group general practices in 24 towns in England, Wales, and Scotland in 1978-80 and from the cohort of the British Regional Heart Study.[4] Patients attending the BUPA medical centre in London appear to have a similar distribution of blood cholesterol to that of the British men reported on here.[5]

Direct application of the American recommendations for high risk (>6·72 mmol/l) and moderate risk (>6·21 mmol/l) blood cholesterol values to the British middle aged male population would result in 31% being treated intensively by dietary means, with drugs being added if response to diet was inadequate. A further 18% of British middle aged men would be treated intensively by dietary means, with a proportion of these requiring drug treatment. Thus, 49% of the British male population aged 40-59 years would require intensive dietary management (table), with all the implications for skilled dietary advice and monitoring of blood cholesterol response. In addition, an undetermined proportion of these would require drug therapy and monitoring of response. The cost implications are staggering.

Included in the NIH consensus development conference statement is the recommendation that "all physicians should be encouraged to include, wherever possible, a blood cholesterol measurement on every adult patient when that patient is first seen." In the British debate on the best policy to be adopted to identify people at most risk for ischaemic heart disease it has been suggested that "we should aim at identifying those above the eightieth percentile of the distribution of serum cholesterol concentrations . . . for that population for which it is planned to give advice."[6] In the United States this policy identified 49% of those who died of coronary heart disease during five years' follow up, and the 90th percentile identified 30%.[6] In British middle aged men use of the 80th percentile would identify only 32% of those who would subsequently develop coronary heart disease (fatal and non-fatal) and use of the 90th percentile would identify only 18%.[7] It seems clear that in British middle aged men the concentration of blood cholesterol alone is not a very good predictor of major coronary heart disease in the next few years.

Blood total cholesterol (mmol/l) in American and British men aged 40-59 years

	Centiles						
	5	10	25	50	75	90	95
American*	4·02	4·31	4·81	5·38	6·01	6·65	7·08
British	4·7	5·0	5·5	6·2	6·9	7·6	8·0

*The values for men aged 40-59, given here, differ slightly from those for all men aged over 40 given above.

Conversion: SI to traditional units—Cholesterol: 1 mmol/l≈38·6 mg/100 ml.

The question of measuring blood cholesterol values for assessing risk in individuals will continue to be debated. What is certain is that blood cholesterol concentrations in British men are high and constitute a considerable risk for ischaemic heart disease. The high risk approach in the United States and Great Britain would appear to have severe limitations. Given the present distribution of blood cholesterol concentrations in British men, nothing short of a population approach is likely to be effective, and even that would have to be applied from childhood if it is to have much effect.

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Co-trimoxazole toxicity

SIR,—The Committee on Safety of Medicines has recently circulated doctors with information on deaths associated with the use of co-trimoxazole (trimethoprim and sulphamethoxazole) and trimethoprim alone. In it the committee states that it would be unwise at this stage to assume that trimethoprim is substantially less liable to cause fatal adverse reactions than co-trimoxazole. No discussion is given to the well known toxicity and fatalities associated with sulphonamides. This is regrettable since most of the deaths associated with the use of co-trimoxazole are typical of sulphonamide toxicity—blood dyscrasias (50 deaths) and skin reactions (14). When sulphonamides are used alone about one case of Stevens-Johnson syndrome occurs per million prescriptions[1] and the incidence of agranulocytosis is about 0·1-0·3%,[1-3] although not all of the latter cases are fatal. Furthermore, clinical trials have shown that other toxic reactions are commoner with co-trimoxazole than with trimethoprim.[4-6] In vitro, human and murine haematopoiesis is inhibited to a greater extent by co-trimoxazole than by either trimethoprim or sulphamethoxazole.[7]

The question of differential toxicity between co-trimoxazole and trimethoprim is now an important issue since the preparation is widely prescribed and many clinical studies suggest that all the antibacterial activity of co-trimoxazole in vivo results from only the trimethoprim component.[8-10] A recent study could not identify any sulphamethoxazole in sputum or saliva during or after a course of co-trimoxazole.[11] So far as we are aware none of the many comparative trials in urinary and respiratory infections that have been performed have provided convincing evidence that the addition of sulphamethoxazole to trimethoprim is of benefit. Moreover, if a patient does develop a toxic reaction after co-trimoxazole it is unwise to prescribe either of the component drugs on subsequent occasions. Speculation that the sulphonamide component of co-trimoxazole protects against selection of resistance has not been supported by clinical studies.[12,13]

From the data presented by the CSM an immediate withdrawal of the drug in the elderly seems warranted, and we would urge the CSM to consider removing the product licence for many other indications. Trimethoprim and a sulphonamide may still be indicated for certain specific conditions—for example, in the management of *Pneumocystis carinii* infection. If so, then surely the selection of a sulphonamide and its dose should be made independently of the trimethoprim moiety, based on the particular patient, notably his renal function? Co-trimoxazole may still occasionally be useful in sexually transmitted diseases and could be prescribed by the appropriate specialists.

We believe that the CSM has not presented us with an accurate appraisal of the information. It would seem reasonable to expect greater toxicity from the combination of two dissimilar drugs than either single agent.

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A somatic component to myocardial infarction

SIR,—I was interested to read the report by Professor Alexander S Nicholas and others (6 July, p 13) describing palpable paravertebral soft tissue changes in patients recovering from acute myocardial infarctions. They conclude that the observed palpable soft tissue changes are specific to patients recovering from acute myocardial infarction. They further claim that these changes may help in diagnosing infarction or in predicting an impending infarction. I see no justification for such conclusions. The paper appears to have several major flaws. The control and study groups were not matched in many important ways and this means that no conclusions can be drawn from the observed differences.

The study group comprised 25 patients recovering from an acute myocardial infarction who were examined within three to five days of the event. The control group included eight (36%) normal volunteers and only six (27%) who were conceivably acutely ill (one patient each with pneumonia, subarachnoid haemorrhage, cholecystitis, thrombophlebitis, pancreatitis, and pulmonary abscess). The difference between the number of acutely ill patients in each group was highly significant ($p<0·0001$ exact test) and important. When ill patients are confined to bed, as they would be after acute myocardial infarction, skin blood flow changes, as does underlying skin nutrition, especially in areas of pressure—for example, heels, buttocks, and thoracic spine. This results in erythema and eventually skin loss. Early changes may possibly be felt as "skin warmth" and "firmness." Ambulant patients would not be expected to have such changes.

Acute myocardial infarction is a dramatic and painful event and is associated with increased sympathetic activity. It is feasible that such activity may have somatic manifestations. Indeed the concept of somatisation of anxiety mediated by the autonomic nervous system is not new—for example, tension headache, irritable bowel syndrome. Few of the control group were acutely ill and so they were unlikely to have increased sympathetic drive or any somatic changes associated with this.

The authors believe that their observed palpable changes are mediated by the autonomic nervous system. Many drugs interfere with the autonomic nervous system, and again the control and study groups differ. More patients in the control group were taking hypnotics and tranquillisers ($p=0·001$ exact). More patients in the study group were taking diuretics, which may change skin turgor ($p<0·01$ exact), and antianginal drugs ($p<0·0001$ exact). β Adrenergic blockers modulate autonomic nervous responses and decrease skin blood flow. Nitrates and calcium channel blockers are vasodilators and increase skin blood flow and are often associated with oedema and flushing. The palpable changes observed in the study group might have been caused by their medication.

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SIR,—Professor Alexander S Nicholas and his colleagues (6 July, p 13) make some extravagant claims about the information obtained from palpating the thoracic paravertebral soft tissues. While they appear to acknowledge that any changes in consistency of such tissues may reflect alterations in sympathetic tone, which may well be increased after myocardial infarction, they do not make any comment about the number of their patients receiving antianginal preparations who were receiving β blockers. Nor do they comment on whether this group are palpably different from those not receiving β blockers.

One presumes that patients recovering from acute myocardial infarction in an intensive care unit will have been bedfast for the first 48-72 hours and thus pressure effects on the paravertebral tissues must contribute significantly to the authors' findings. I have grave doubts about extrapolating this sort of work to previously ambulant patients presenting with suspected myocardial infarction. Also I have reservations about their control group, most of whom appeared to have conditions which would not prevent them being ambulant; indeed eight were not inpatients.

Finally, I have yet to see any dog that rests on its back and therefore doubt that much can be inferred about soft tissue changes in the human paravertebral area from a canine model.

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** The authors reply below.—ED, *BMJ*.