Serum cholesterol (mmol/l)	Mean (SD) score on general health questionnaire	
	Men	Women
<3.2	22.27 (7.00) (n=11)	33.43 (19.03) (n=7)
3.2-4.2	23.65 (10.25) (n=71)	21.95 (11.12) (n=64)
>4.2	21.50 (8.21) (n=40)	25.00 (12.22) (n=81)

*Data not available for some patients.

and questionnaire scores, but a subgroup of women—namely, those with low cholesterol concentrations (lowest 5% of the population)—had significantly poorer mental health as indicated by their questionnaire scores ($p < 0.04$).

Although we found a significant relation only in the women, these data support the suggestion that low cholesterol concentrations may be associated with altered mood. The difference between the sexes was unexpected as the impact of changes induced by diet or drugs has tended to be studied in men, and Lindberg and colleagues found an association between cholesterol and suicide only in men.¹ Our study, however, was of subjects younger than those in similar studies. Our finding, in a relatively small sample, suggests that use of similar psychological methods, rather than the rate of suicide, may allow this topic to advance more rapidly. Our data suggest that particular attention should be directed at those with low cholesterol values.

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- 1 Lindberg G, Rastam L, Gullberg B, Eklund GA. Low serum cholesterol concentration and short term mortality from injuries in men and women. *BMJ* 1992;305:277-9. (1 August.)
- 2 Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. *BMJ* 1990;301:309-14.

EDITOR,—In their long term follow up of adults who participated in the Värmland survey in Sweden, Gunnar Lindberg and colleagues report a significantly higher incidence of suicide and violent deaths in middle aged and elderly men whose cholesterol concentrations were in the lowest quarter of those surveyed.¹ This difference in violent deaths was limited to the first seven years of follow up. A cause and effect relation is suggested.

Suicide and risk taking behaviours are most commonly found among middle aged or elderly men with psychological depression.^{2,3} Loss of appetite and weight loss are characteristic of this state or illness,^{3,4} and loss of over 5% of body weight is regarded as one of the diagnostic characteristics of acute depressive illness.³ Weight loss is strongly associated with a fall in serum total cholesterol concentration.^{5,6}

Among middle aged men 2.5-3.2% are estimated to have an acute depressive illness at any one time,³ while others may suffer from reactive depression based on losses and social misfortune.^{2,4} Thus in the Värmland study a sizeable group of men might be expected to have been depressed at the time of the survey. Most of these would have recently lost weight or been losing weight. For many of them their cholesterol concentrations would have fallen, or been falling, into the lowest quartile at that time. They would be at risk of violent death from suicide or risk taking behaviours during the ensuing months or few years.^{2,3}

Lindberg and colleagues found no relation between low cholesterol concentrations and suicide in women. Depressed women are much less likely to commit suicide than are depressed men.^{2,3} The authors noted no significant interaction between cholesterol concentrations and suicide with age. They do not report the relation between cholesterol

concentrations and body mass index in the survey, although body mass index was included in the survey.⁷

What the study probably indicates is that men who met violent deaths, commonly from suicide, had been depressed for some time beforehand and, because of weight loss, had lower serum cholesterol concentrations.

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- 1 Lindberg G, Rastam L, Gullberg B, Eklund GA. Low serum cholesterol concentration and short term mortality from injuries in men and women. *BMJ* 1992;305:277-9. (1 August.)
- 2 Stengel E. *Suicide and attempted suicide*. Revised ed. Harmondsworth, Middlesex: Penguin, 1970.
- 3 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, third edition*. Washington, DC: American Psychiatric Association, 1987.
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- 5 Kromhout D. Body weight, diet and serum cholesterol in 871 middle-aged men during 10 years of follow-up (the Zutphen study). *Am J Clin Nutr* 1983;38:591-8.
- 6 Tuomilehto J, Salonen JT, Nissinen A. Factors associated with changes in serum cholesterol during a community-based hypertension programme. *Acta Med Scand* 1985;217:243-52.
- 7 Lindberg G, Eklund GA, Gullberg B, Rastam L. Serum sialic acid concentration and cardiovascular mortality. *BMJ* 1991;302:143-6.

DITOR,—The paper by Gunnar Lindberg and colleagues provides support for a link between low serum cholesterol levels and suicide.¹ Although the authors comment that the causality of the link is unresolved, we think that several points should be noted.

Lipid was measured as single random serum total cholesterol concentration; allowance is therefore needed for day to day intrapatient variation of up to 11%² and the influence of seasonal or other factors. It would be desirable to see data on high density lipoprotein and low density lipoprotein cholesterol to put the association in similar terms to those used in ischaemic heart disease. This may also provide evidence for the confounding effect of alcohol misuse, which is shown to increase high density lipoprotein cholesterol.³

We propose several other confounding variables: a highly energetic and active lifestyle, while lowering cholesterol, may predispose to fatal accidents; ongoing ill health other than cancer can lower total cholesterol concentrations and may give rise to depressive illness and thus increase the risk of suicide.

We emphasise that the findings of this study do not establish a causal relation between suicide and low cholesterol. It is equally possible that people in this Swedish study who were likely to commit suicide may have had low cholesterol levels due to their depressive nature and physical state.

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- 1 Lindberg G, Rastam L, Gullberg B, Eklund GA. Low serum cholesterol concentration and short term mortality from injury in men and women. *BMJ* 1992;305:277-9. (1 August.)
- 2 Demacker PNM. Intra-individual variation of serum cholesterol, triglycerides and high density cholesterol in normal humans. *Atherosclerosis* 1982;45:259-66.
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AUTHORS' REPLY,—We concluded firmly that although our results supported an association between the risk of suicide and cholesterol concentrations in men, the direction of this relation was not resolved. We were hesitant to speculate too far on this, but several explanations have been brought up in this correspondence.

David Benton and Joyce Fordy suggest that low cholesterol concentration is associated with low mood. Even though their own data provided no support for this in men it is thought provoking, especially in the light of a recent hypothesis about poor suppression of harmful behavioural impulses in subjects with low cholesterol.¹

Alan J Goble and Marian C Worcester suggest that we try the possible confounder of loss of appetite in the depressive state, by adjusting for body mass index. The correlation between total cholesterol and body mass index in our cohort as well as in other populations was low ($r = 0.11$ in men), and thus it is unlikely that this analysis should provide any new information. As they state, there is a higher correlation between weight change and cholesterol change, but only one recording of these two variables is available in the Värmland study, and thus no correction is possible.

Confounding from a highly energetic and active lifestyle is a different possibility, worth investigating in future studies. The same is true for ill health, which we ruled out as far as possible by excluding subjects included on the registry.

All these explanations are, as far as present knowledge allows us to conclude, equally probable and should if possible be addressed in future studies of the impact of total cholesterol concentration on disease incidence and mortality.

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- 1 Engelberg H. Low serum cholesterol and suicide. *Lancet* 1992; 339:727-9.

Vaccination against *Haemophilus influenzae b* disease

EDITOR,—Keith A V Cartwright states that *Haemophilus influenzae b* vaccine may be given concurrently with diphtheria, tetanus, and pertussis vaccine or with measles, mumps, and rubella vaccine into a different limb.¹ The latest edition of the handbook on immunisation against infectious disease agrees with this and adds that the sites of injection should be recorded.² In the event of any local reaction, confusion may arise as to the responsible vaccine unless it is both clearly recorded in the notes and the child's parents are aware which vaccine has been given in which site. In York Health Authority, to avoid this potential problem, we are currently recommending that *H influenzae b* vaccine should always be given in the right limb, with the other side being available for other vaccines. Other health authorities may wish to follow suit.

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- 1 Cartwright KAV. Vaccination against *Haemophilus influenzae b* disease. *BMJ* 1992;305:485-6. (29 August.)
- 2 Department of Health. *Immunisation against infectious disease*. London: HMSO, 1992.

Site of injection for vaccination

EDITOR,—Colin Payton illustrates the validity of my concern over the misconception of many who administer vaccines that the deltoid area is a superior site for injection.¹

There are no data comparing vaccine absorption in the muscles of the deltoid region and the anterolateral aspect of the thigh, but there is no valid reason to suspect that any differences exist.

The reason given by the manufacturers for the alternative sites recommended for children and adults is simply that these were the sites used in the trials of the vaccine (SmithKline Beecham, personal communication). The only indications for administration of hepatitis B vaccine into the upper arm are thus convention and convenience.

Overweight adults generally have a problem with subcutaneous fat on the arms as well as the legs and, although the anterolateral aspect of the thigh may be more severely affected, the number of health service workers in whom this precludes an intramuscular injection is small. The anterolateral aspect of the thigh requires penetration of fascia lata to enter muscle and the feeling of "give" resulting from passage of the needle is a better indicator of the correct site for injection than anything available in the upper arm. It is also easier to differentiate between the buttock and anterolateral aspect of the thigh than between different sites over the deltoid and upper arm.

Work is currently in progress at the Communicable Diseases Surveillance Centre to identify whether any site of injection carries an increased risk of local reaction; the lack of accurate denominator data (numbers of children immunised at different sites) may make this difficult to complete (N Begg, personal communication). Any loss of skin continuity in the upper arm and deltoid region will, however, be more likely to scar badly and will definitely be more obvious than on the anterolateral aspect of the thigh. In an increasingly litigious population the use of a site where any penetrating injury can result in unsightly scars or keloid formation with no apparent advantage to the patient must be questioned.

All patients should be advised of the alternative sites available for vaccination by intramuscular injection; many will prefer the upper arm but the choice should be theirs.

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1 Payton C. Site of injection for vaccination. *BMJ* 1992;305:364. (8 August.)

Early treatment of meningococcal disease

EDITOR,—We recently presented data from five health districts on the effect of early treatment with parenteral penicillin on mortality in suspected meningococcal disease.^{1,2} Although in each district there was a lower mortality in those treated early, the reductions in mortality failed to reach significance. As case definitions in the studies were comparable we tested the effect of combining data on the 487 patients from the three published reports.

The overall case fatality was 9.7% (47/487). A total of 358 patients did not receive parenteral penicillin before admission, of whom 41 (11.5%) died; by comparison, six deaths (4.7%) occurred among the 129 patients who received parenteral penicillin before transfer to hospital. The risk of death in patients not given parenteral penicillin was significantly increased (Mantel-Haenszel weighted odds ratio 2.61; 95% confidence interval 1.04 to 7.18). These data confirm the benefit of early antibiotic treatment.

The early diagnosis of meningococcal disease may present formidable problems in general practice. Individual doctors will see few cases in their professional lifetime, even in districts with a high incidence. Early symptoms are non-specific, and up to 40% of patients may not develop a rash in the period before admission to hospital. The diagnosis was, however, suspected in over three quarters of patients seen by a doctor before transfer

to hospital in the Darlington study.¹ We encourage our general practitioner colleagues to carry benzylpenicillin at all times and to give it without hesitation if meningococcal disease is possible.

Public health physicians with special responsibility for communicable disease control can influence rates of giving penicillin.^{1,2} Departments of public health medicine are well placed to collaborate with microbiologists and hospital physicians to mount information and alerting campaigns directed at local family doctors to sustain awareness of meningococcal disease and to recommend early use of parenteral penicillin. Application of this strategy nationwide could have a considerable impact on the case fatality rate from meningococcal disease.

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- 1 Strang JR, Pugh EJ. Meningococcal infections: reducing the case fatality rate by giving penicillin before admission to hospital. *BMJ* 1992;305:141-3. (18 July.)
- 2 Cartwright K, Reilly S, White D, Stuart J. Early treatment with parenteral penicillin in meningococcal disease. *BMJ* 1992;305:143-7. (18 July.)
- 3 Gossain S, Constantine CE, Webberley JM. Early parenteral penicillin in meningococcal disease. *BMJ* 1992;305:523-4. (29 August.)

EDITOR,—Two recent papers have analysed the relation between antibiotic treatment given before admission to hospital and mortality from meningococcal disease and found a trend with fewer deaths among patients receiving parenteral antibiotics before admission.^{1,2}

We have just made a historical cohort study including all 177 patients who were admitted with meningococcal disease to hospitals in the county of North Jutland, Denmark, between 1 January 1980 and 31 December 1989.³ As part of this investigation we analysed the relation between prehospital parenteral antibiotic treatment and death from meningococcal disease.

The standard recommendations of the Danish health authorities regarding prehospital treatment of meningococcal disease are that penicillin G should be given intravenously (or intramuscularly if the intravenous attempt is not immediately successful) when petechiae or other signs of meningococcal sepsis are present, and if the patient shows signs of severe meningitis and the transport time to the nearest hospital is more than half an hour.

When the general practitioner suspected meningitis (in 123 of the 177 patients) the recommendations for immediate antibiotic treatment should have been followed. Of these 123 patients, 98 should have had parenteral antibiotic treatment before admission to hospital. In fact only 25 had treatment according to recommendations.

Of the 98 patients, 10 died: six of the 25 patients who received parenteral antibiotics and four of the 73 patients who did not receive parenteral antibiotics before admission. The higher mortality in the parenteral antibiotic group is statistically significant ($p=0.03$, Fisher's test) with odds ratio of 5.4 (95% confidence interval 1.5 to 19.2).

Of the 177 patients in the study, a total of 11 died: six of 25 patients receiving parenteral antibiotic before admission and five of 152 not receiving parenteral antibiotics before admission. The difference in mortality is statistically significant with odds ratio of 9.3 (3.1 to 27.9).

Overall 11 patients died in our study. Ten of 15

patients with disseminated intravascular coagulation died, whereas only one patient died out of 162 without disseminated intravascular coagulation. Using logistic regression analysis on the whole study population we found that only the presence of disseminated intravascular coagulation predicted death with statistical significance ($p<0.001$) with an odds ratio for death of 170 (15 to 1930).

The high mortality (24%) among the patients who received prehospital treatment with parenteral antibiotics was probably due to a particularly fulminant infection, easily recognisable at home. Thus, our study shows the opposite tendency to the two British investigations. To further elucidate the role of parenteral prehospital antibiotic treatment it seems necessary to evaluate the severity of the meningococcal disease at the time of decision to give the treatment. We recommend stratified analysis taking this into account in future investigations.

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- 1 Strang JR, Pugh EJ. Meningococcal infections: reducing the case fatality rate by giving penicillin before admission to hospital. *BMJ* 1992;305:141-3. (18 July.)
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- 4 [The State Serum Institute: meningococcal disease/purulent meningitis.] *EpiNyt* 1984;week 32. (In Danish.)

Controlling leprosy

EDITOR,—Christian Lienhardt and P E M Fine do not believe that using multidrug treatment alone will achieve the World Health Assembly's goal of eliminating leprosy as a public health problem by the year 2000.¹ They do accept, however, that "dramatic falls in the incidence of leprosy (or case detection rates) have been documented [which] began in most countries long before the introduction of multidrug treatment" but attribute this decline to "improving socioeconomic standards" and BCG vaccination.¹ They ignore completely the effect of dapsone monotherapy in interrupting transmission despite evidence from northern Nigeria, Uganda, India, and central Burma.²

In striking contrast, none of the patients in Karimui, New Guinea, originally received any chemotherapy and the incidence of the disease remained constant at 5/1000 from 1964 to 1969.³ A BCG vaccine trial started there in 1964; the final results were expressed in incidence per 1000 person years⁴ and the significance of the findings has been missed. In November 1967 chemotherapy was started with acedapsone, a long acting sulphone.⁵ Incidence rates can be calculated in vaccinated and unvaccinated groups from the cumulative totals previously published,^{4,5} and the considerable decline in unvaccinated groups (figure) must be attributable to chemotherapy. Furthermore, only one new patient in the unvaccinated group^{4,5} was detected after 1972 with