found between contamination of the catheter and local inflammation but it would have been interesting to determine whether there was any correlation between the incidence of local inflammation and the number of times the side port had been used. The introduction of a number of organisms directly into the bloodstream of a fairly healthy person is unlikely to do harm but it might lead to general infection in cases where the general level of immunity is reduced or where there exists some site particularly susceptible to infection, such as a damaged heart valve.

No adequate controls appear to have been used in this survey; the comparison of inflammation rates with those obtained by different workers in other countries under different circumstances cannot be regarded as valid. That only controls examined in parallel are suitable comparisons is supported by the conclusion that the complication rates for phlebitis (35%) are said to be no higher than those reported for continuous-flow cannulae used for fluid or heparin infusion, whereas Peters *et al*¹ mentions a figure of 20%, a discrepancy in the total number of cases in the UK of 1.5 million per year.

Oberhammer² (also personal communication) has shown to what degree the injection ports of cannulae may be contaminated; such ports are not really necessary, and while there is any suspicion that they may constitute a danger it seems illogical to use cannulae bearing them unless there are special indications.

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¹ Peters JL, Fisher C, Mehtar S. *Lancet* 1980;ii:1028.
² Oberhammer EP. *Lancet* 1980;ii:1027.

SIR,—We read with interest the observations of Dr J T Macfarlane and others (22 November, p 1395) regarding the incidence of thrombophlebitis and bacterial growth from the tips of Venflon cannulae used for intermittent or continuous intravenous therapy. This cannula has an integral, recessed, and valved side port for intermittent intravenous injection using a syringe without the need for a needle. The injection port unfortunately acts as a sump, retaining a meniscus of fluid, and cannot be cleaned before or after the injection procedure. This potentially dangerous design feature has been emphasised originally by Pilsworth¹ and subsequently by us.²⁻⁴

We note that Dr Macfarlane and his colleagues have not described their insertion or dressing technique; they cultured the cannula tip, but do not mention the results of culturing the side port during or at the end of cannula usage. Oberhammer has recently performed such a study; and he showed 31 out of 56 (55%) cannulae with injection ports to have bacterial colonisation, using impression inoculation and rinse culture techniques from the lumen of the side ports.⁵ Infection introduced from here might well be flushed into the vein, with a conceivably negative culture from the cannula tip. Dr Macfarlane and others have reported morbidity and mortality, which should stimulate the search for improvements. Their figure of 5 million cannulae a year in use in Britain suggests that the number of people at risk from bacterial infection from intravascular devices may be 750 000. Their experience of one fatal case of septicaemia and endocarditis as a consequence of an intravenous cannula is not unique,⁶ and many more must occur throughout the country. Indeed, Oakley has recently emphasised that the true incidence of

infective endocarditis in Britain is unknown because it is not a notifiable disease.⁷

Finally, the authors report a 35% incidence of phlebitis following intravenous cannulation. To Cruveilhier,⁸ phlebitis following the wounding of a vein meant sepsis and he considered that this was the most common source of sepsis that he saw at necropsy. Over 100 years later the problem is still of considerable magnitude. Clearly every step should be taken to eliminate such potential and actual sources of morbidity and mortality in hospital practice. What is the point of the manufacturing pharmaceutical and plastics industry spending vast sums to ensure that every syringe and ampoule of a drug for intravenous administration is sterile if these are to be filled and injected through a port in which there is a 55% incidence of pathogenic bacterial contamination? There can be few diseases in which the patient will benefit from intermittent intravenous injections of bacteria. We have already pointed out that the Venflon cannula is not sold in the USA.⁴ Does the cannula meet the requirements of the 1976 Medical Device Amendments Legislation, which broadened the powers of the Food and Drug Administration Bureau of Medical Devices? What are British Viggo's own statistics on bacterial colonisation in side ports?

The danger of monitoring devices as a cause of septicaemia has been emphasised in a *BMJ* editorial.⁹ We believe that similar design configurations placed in infusion lines carry the same risks; and our views may be summarised in the aphorism, "Stopcocks do not stop cocci from entering the circulation, and injection ports provide a fine harbour for micro-organisms."³ Industry needs to provide improved alternative devices for the future which do not sequester bacteria in this way. We agree with Oberhammer⁵ that companies should discontinue manufacturing devices with injection ports which cannot be safely and repeatedly disinfected.

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² Peters JL, Fisher C, Mehtar S. *Lancet* 1979;ii:1239.

³ Peters JL, Fisher C, Mehtar S. *Lancet* 1980;iii:701.

⁴ Peters JL, Fisher C, Mehtar S. *Lancet* 1980;iii:1028.

⁵ Oberhammer EP. *Lancet* 1980;ii:1027.

⁶ Stronge JL, Meers PD. *Nursing Times* 1980; October, suppl:114-5.

⁷ Oakley CM. *Br J Hosp Med* 1980;September:232.

⁸ Cruveilhier J. In: Long ER, ed. *Selected readings in pathology*. Springfield, Illinois: Charles C Thomas, 1929:217.

⁹ Anonymous. *Br Med J* 1979;i:1748.

* * * We sent this letter to British Viggo, whose reply appears below.—Ed, *BMJ*.

SIR,—I would like to reply to the letter by Mr Peters and others, which is in a similar "vein" to their previous letters on the subject.¹⁻³

Noble *et al*⁴ have shown an incidence of cannula tip colonisation as low as 12.5% for Venflon cannulae, which is no higher than the mean incidence of 25% (range 3.8–57%) cited by Maki⁵ in his evaluation of cannula-associated problems. Noble also concludes that the frequency of inflammation in his study on Venflon cannulae agrees with previously published reports, and at 20% this is also no higher than the average rate (24.7%) quoted

by Maki.⁵ Noble classified inflammation into grades I, II, and III (in increasing severity). Of the 20% inflammation found by Noble there were no cases of grade III (suppurative phlebitis) and only 3% were classed as grade II, leading Noble to conclude that "inflammation, in this study, was for the most part mild."

More recently, the prospective study by Dr MacFarlane and others has been published which, in addition to confirming similar complication rates for Venflon Cannulae to those found by Noble, also studied the relationships between cannula tip isolates and infection at the site of entry. Phage typing, Bio typing and antibiograms of these isolates suggested that in the majority of instances the bacteria originated from the patient's own skin. Further independent work on this subject is awaiting publication and we feel that this will be more credible than publication of our own findings.

We accept that there is a potential hazard with the use of any intravenous device but intravenous therapy is now an accepted form of medical practice. It is surely the responsibility of both the manufacturers and the user to minimise such risks. However, in looking at the hazards it is important to review the published evidence concerning the clinical use of such devices. Venflon, when used either for continuous infusion⁴ or for intermittent administration as in the recent *BMJ* study, has shown complication rates for phlebitis, cannula tip positive cultures, and bacteraemia no higher than for other intravenous cannulae.⁵

Venflon is not sold in the United States but a similar product—Vasculon—is registered for sale by the Food and Drug Administration both with and without a Venflon-type injection port.

We are becoming increasingly convinced that the major factor affecting venous complications of all cannulae is the "housekeeping" associated with the procedure, and as a company we are continuing to do our utmost to help in this area. However, if Mr Peters and others have conclusive evidence of clinically significant complications which disagree with the findings of Maki,⁵ Noble,⁴ and MacFarlane (and other published work) then we would be very interested to discuss this further.

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¹ Peters JL, Fisher C, Mehtar S. *Lancet* 1979;ii:1239.

² Peters JL, Fisher C, Mehtar S. *Lancet* 1980;iii:701.

³ Peters JL, Fisher C, Mehtar S. *Lancet* 1980;iii:1028.

⁴ Noble CJ, Morgan-Capres P, Hammer M, *et al*.

J Hosp Infect 1980;i:47-51.

⁵ Maki DG, Goldmann DA, Rhame FS. *Ann Intern Med* 1973;79:867-87.

Effects of high dietary sugar

SIR,—The decline of high density lipoprotein (HDL) cholesterol concentrations in people with a high dietary sugar noted by Professor J Yudkin and colleagues (22 November, p 1396) is perhaps the most important point in their data which needs emphasis. The mechanism by which high dietary sugar reduces the protective HDL cholesterol is not clear. Earlier epidemiological and experimental studies including my own¹⁻⁴ were critical of the sucrose hypothesis. Does high dietary sucrose also influence the relative proportion of long-chain versus short-chain fatty acids in the blood? The preponderance of long-chain (C₁₈₋₂₁ series) fatty acids in the blood is an important risk factor.^{4,5} It depends upon:

(a) the chain length of fed fats⁶; (b) pattern of food^{1 3 4} (fibre-rich or fibre-poor); (c) the manner of eating⁵ (masticatory or non-masticatory); and (d) the method of cooking.^{2 5}

The relative preponderance of long-chain (C_{18-21}) versus short-chain (C_{4-6}) fatty acids and not the total cholesterol concentration has been shown to play an important part in blood clotting and clot-lysis.^{7 8} Plasma freed from chylomicrons, the end product of long-chain fatty acids, failed to clot. But when washed chylomicrons were returned to the plasma substrate normal clotting was restored.⁹

Since clearly it is not the total cholesterol concentration but the relative proportion of long-chain versus short-chain fatty acids, the density of chylomicrons, or the level of HDL versus low density lipoprotein cholesterol and very low density lipoprotein cholesterol which are reliable indicators of coronary heart disease risk, is it not better to stop estimating total cholesterol and to switch on to these, both in epidemiological and in clinical work?^{4 5} There is the added advantage that technological improvements in gas chromatography and the new precipitation tests for HDL-cholesterol make their estimation much easier than the estimation of the less informative and also less dependable total cholesterol concentration.

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¹ Malhotra SL. *Am J Clin Nutr* 1967;20:462-74.

² Malhotra SL. *Br Heart J* 1967;29:334-44.

³ Malhotra SL. *Br Heart J* 1967;29:895-905.

⁴ Malhotra SL. *Br Heart J* 1973;1:17-23.

⁵ Malhotra SL. *Am J Clin Nutr* 1971;24:1195-8.

⁶ Ahrens EH Jr, Hirsch J, Insull W Jr, Paterson ML. In: *Chemistry of lipids as related to atherosclerosis*. Springfield: Thomas 1958:222.

⁷ Connor WE, Poole JCF. *Quart J Exp Physiol* 1961;46:1.

⁸ Malhotra SL. *Br Heart J* 1968;3:303-8.

⁹ Poole JCF. *Fed Proc* 1962;21:suppl No 2,20.

Nalidixic acid in pregnancy

SIR,—Professor A W Asscher (21 May 1977, p 1332) stated that nalidixic acid should be avoided in the late stages of pregnancy since it may produce hydrocephalus in the fetus even in low dosage. This opinion was presumably based on reports such as that of Deonna and Guignard,¹ who described two infants who developed hypertension during treatment of their urinary infections with nalidixic acid.

From 1975 we have kept records in our laboratory of each woman in Ayrshire who has had a urinary infection during pregnancy, information about dose and duration of antibiotic treatment being obtained by means of a request form sent along with the microbiology results to the doctor concerned. From these records we have traced 63 women who were treated with nalidixic acid during pregnancy. The medical condition of the children born to these mothers was checked during the neonatal period and at 1 year.

Of these 63 women, six were treated with nalidixic acid during the first trimester, 26 during the second trimester, and 30 during the third trimester; the remaining woman was treated at term (commencing 48 hours before delivery). The standard dose of 1 g nalidixic acid four times daily for 7-10 days was given to 44 of the 63 women and eight were given 0.5 g four times daily for a similar period; for the remaining 11 the dose was unspecified.

Of the 63 children, 61 showed no evidence of congenital abnormality or intracranial hypertension during the neonatal period. At 1 year of

age 60 of these 61 showed no congenital abnormality and no evidence of intracranial hypertension. The records of the remaining child could not be traced. Two of the 63 infants died in the neonatal period, one with hyaline membrane disease after delivery at 34 weeks' gestation and the other with a severe congenital heart condition. The mother of the latter child had a bicornuate uterus and congenital dislocation of the right hip. Of her seven pregnancies, two had ended in abortion at 10 weeks; two (including the current one) had produced congenitally abnormal infants who had died (the earlier one with cebocephalus) and she had three live children. Genetic counselling had been considered after the delivery of the grossly abnormal infant in 1974, but for various reasons this was not pursued. Since this woman received nalidixic acid at the beginning of the third trimester, treatment would appear to be unrelated to the cardiac deformity.

We therefore conclude that in none of these 63 pregnancies did the administration of nalidixic acid to the mother appear to cause congenital deformity or intracranial hypertension in the child.

I wish to thank Dr Ian Ruthven, consultant paediatrician; Dr David Paterson, community medicine specialist; and the staff of the community medicine department for clinical assessment of the children.

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Comparison of neonatal management methods for very low-birth weight babies

SIR,—The death rate of babies weighing 1-1½ kg is a convenient indicator of the fate of babies as a whole. Their numbering is likely to be accurate as they will not be dismissed as too small to count or too large for special care; and both their mortality and their survival are large enough to reflect small changes in their care before and after birth.

Your correspondents (29 November, p 1488-90) and others^{1 2} report the recent mortality of such babies born in their hospitals as about 20% (University College Hospital 18.5%, Aberdeen 22.1%, Belfast 18%, Cambridge 24%, Harvard 18%). Although the individual numbers are small and the mortality has a one in 20 chance of being 10% higher, there seems to be a genuine difference from the 35% mortality of a few years ago. This they attribute to more intensive care. In Salisbury³ in 1973-6 a corresponding series of babies, who were not treated invasively, had a mortality of 21%; 11 of 388 babies weighing 1½-2½ kg died, which is near to Belfast's figure of 9 in 390 for 1978-9; and the adjusted perinatal rate of Chalmers *et al*⁴ for 1976 showed Wiltshire (which includes Salisbury), Oxfordshire (which includes Oxford), and Camden and Islington (which include University College Hospital) to have the lowest figures in England and Wales at 11.01%, 10.49%, and 10.35% respectively. The figures of Chalmers also show that although Oxford City had a low mortality it was one of only four areas in England to show a rise in mortality in 1965-73 against a national fall of 0.73/1000 per year.

How can this be explained? It at last seems to be agreed that intensive care as practised in even the best centres 10 years ago did little to help the babies. (In Hammett-smith only one baby of 19 weighing under

1 kg born from 1971 to 1975 is not either dead or mentally subnormal⁵; and the arrest of Oxford's figures followed a decade or more of rigorous obstetrics and gentle paediatrics.) We are told now, as we were told then, that intensive care should spread; but King's Mill's latest figures, which Professor E O R Reynolds and Dr Ann L Stewart (p 1488) find unacceptable, were the result of just such a spread and the ending of old ways. The millennium may have come, and certainly for the few babies under 1 kg there seems some hope where there was none before; but it has not yet been proved. As a first step birth notifications should bear birth weights, and figures should be published by hospital of birth as well as by administrative area.

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¹ Robertson NRC. *Lancet* 1979;iii:362.

² Brown E, Tacusch HV. *Lancet* 1979;iii:362.

³ Hughes-Davies TH. *Arch Dis Child* 1979;51:59-61.

⁴ Chalmers I, *et al*. *Health Trends* 1978;10:24-8.

⁵ Jones RAK, Cummins M, Davies PA. *Lancet* 1979;ii:1332-5.

SIR,—Recent correspondents in your columns, critical of the paper by Dr E S Steiner and others (8 November, p 1237), failed to compliment the authors on a major achievement: presenting their results so cleverly that they actually appeared to support a policy of non-intervention.

Firstly, as others have noted (29 November, pp 1488-90), the authors compared their results with those of London neonatal units in the sixties and early seventies, carefully avoiding any reference to the greatly improved results now being achieved with improved techniques and equipment. They then made three subtle adjustments to their data to enable them to support their Spartan approach with an impressive figure for total handicap of 17.8%. That others might marvel, we will explain. In their summary they state that 5.5% of their study group had a major handicap and 12.3% a minor handicap and 30.5% were normal. Those adept at mental arithmetic will note that these figures add up to 48.3%, for the authors have represented their figures as proportions of the whole study population living and dead, so taking full advantage of their high mortality rate. It is usual practice, of course, to present handicap figures as a percentage of survivors; of their 236 babies born in the labour ward, half died. Of the 114 traced long-term survivors, 13 were severely handicapped and 29 had minor handicaps: a handicap rate of 36.8%.

A detailed look at their results reveals further ingenuity. Table IIIm lists details of 18 children with major handicap and they refer to 31 cases of minor handicap. The basis of this discrepancy is the phrase "liveborn in the labour ward." Most units, when presenting their data, exclude correctly those infants born in distant hospitals and referred for special care, so as to give a more accurate epidemiological picture. Not surprisingly, King's Mill Hospital did not receive such referrals and all 293 infants studied came from their own "geographically defined community." Unfortunately, the 57 born outside the labour ward fared rather worse than the others and when they are included the death rate becomes 53.2%. Among the 131 traced survivors of the whole group, 13.7% had a major handicap. With the 31 minor handicaps, the new overall figure for handicap becomes 37.4%.

The clue to the third adjustment lies in the arithmetic of the paragraph on learning difficulties. One hundred and twenty-two of the 131 survivors had been assessed by the Neale reading analysis and Wechsler intelligence tests, which revealed 63 children with a reading age two or more years below average. Table Vm tells those with acute vision that the nine children not tested included five with severe handicaps. If we assume the other 44 "handicapped" children were among the slow