

obtain health authority funding in the current financial year, charging the authority between £530 and £900 per cycle. One of the private units was negotiating to obtain health authority contracts for £1500 per cycle (excluding drugs).

Our NHS trust has elected to exclude *in vitro* fertilisation from block contracts, which are held with 50 or so districts, and it is encouraging that about half of those have so far agreed to pay for this treatment on an extracontractual referral basis, but with a wide variety of "rationing" conditions. The charge for a cycle of *in vitro* fertilisation, including drugs, is roughly £1200, and for tubal surgery as an extracontractual referral the charge is £2639 (but most districts have not excluded tubal surgery from their block contracts).

To help purchasing authorities make rational choices they need to be reminded of expected rates of successful pregnancy from these treatments and to be aware that tubal surgery produces extremely variable success rates (5% to 36%), depending on the severity of the tubal disease, age of the patient, and skill in the surgical technique. The table gives the comparative costs of the two treatments depending on the pregnancy rate.

Comparative costs per baby of *in vitro* fertilisation (IVF) and tubal surgery with different pregnancy rates

Procedure	Cost (£)	Live birth rate (%)	Cost per baby (£)
Tubal surgery	2639	30	8 790
Tubal surgery	2639	5	52 780
IVF, 4 cycles (including drugs)	4800	60 (cumulative)	8 000

Gynaecologists must be highly selective in their approach to tubal surgery if they are to ensure that resources which could be directed to assisted conception more effectively are not wasted on tubal surgery with a poor prognosis.

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- 1 Baird DT. Assisted conception on the NHS? *BMJ* 1992;305:204-5. (25 July.)
- 2 Watson AJS, Gupta JK, O'Donovan P, Dalton ME, Lilford RJ. The results of tubal surgery in the treatment of infertility in two non-specialist hospitals. *Br J Obstet Gynaecol* 1990;97:561-8.
- 3 Larsson B. Late results of salpingostomy combined with salpingolysis and ovariolysis by electromicrosurgery in 54 women. *Fertil Steril* 1982;37:156-60.

EDITOR.—David T Baird's editorial on assisted conception raises the issue of funding for comprehensive infertility services in the NHS.<sup>1</sup> As the director of one of the few NHS units in the United Kingdom, I agree that appropriate resources are urgently needed to support such activities. My experience since the changes in the NHS has been that the decisions relating to funding of assisted conception have now been placed in the hands of the district purchasers, who, unlike the suffering infertile couples, do not see infertility as a priority.

Purchasers are adopting various strategies: many are ignoring extracontractual requests; a few are acknowledging extracontractual requests but making no firm decisions; a minority are refusing outright; and an extreme minority are agreeing to a limited number each year (that is, rationing in their own district). Because purchasers are funding so few extracontractual requests despite the demand from patients (>250 on our waiting list) Guy's Hospital can no longer support a programme of assisted conception on the NHS. Other units associated with the NHS have survived and prospered by becoming private. Reluctantly, we may have to do this too.

The broader issue that needs to be addressed

publicly is that of rationing health services. Rationing has always occurred, but the purchaser-private split highlights the problem. Currently, a small group or perhaps only one public health doctor or manager is making decisions on behalf of infertile couples. Interestingly, we have noticed that the more supportive purchasers have been those with women participating in the decision. Such rationing behind closed doors is against the principle of patients having the power to choose and money following patients. Public debate on this is urgently required.

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EDITOR.—Trevor Sheldon and colleagues present surprisingly negative comments on the effectiveness of infertility treatment,<sup>1</sup> particularly in view of the encouraging messages fronting their review in the most recent issue of *Effective Health Care*.<sup>2</sup> They comment sweepingly about all infertility medicine, though it covers a wide range of distinct disorders, which need specific consideration. Proper balance is required.

A critical review of infertility treatment has been published elsewhere.<sup>3</sup> Controlled studies have shown a lack of therapeutic effectiveness of, for example, hormones or surgical ablation in minor endometriosis and of hormones, artificial insemination, and (generally) microinjection techniques in sperm disorders. Randomised controlled studies are lacking in other conditions, but prospective time specific studies without treatment have shown severe subfertility associated with, for example, infective tubal damage, severe endometriosis, amenorrhoea, and prolonged unexplained infertility. In all those conditions natural conception rates are around 1% each cycle and amount to 10-30% over two years.

Prospective studies of treatments can therefore be reasonably judged by comparison with such well defined, severely reduced rates of natural conception. Furthermore, they can be assessed by comparison with expectations of normal fertile couples—that is, pregnancy rates averaging 20-25% each cycle and amounting to 90-95% after one to two years (or equivalent number of cycles of treatment).

It is now clear that hormonal treatment of amenorrhoea is fully effective; surgery of even the highest quality offers only moderate success in a select minority of cases of tubal damage; and *in vitro* fertilisation to bypass tubal damage offers success rates approaching normal, and the same is true of other assisted conception methods like gamete intrafallopian transfer, which can also be used in endometriosis and prolonged unexplained infertility.

Important differences between natural and assisted conception methods are that assisted conception risks multiple pregnancy—but that is now strictly limited in Britain—and do not involve the same time span. In general, assisted conception is undertaken at most every two cycles and often at longer intervals depending on resources (both NHS and personal).

The fact that such clinical treatments may be undertaken only infrequently, seemingly reducing their effectiveness in terms of time specific pregnancy rates, is not a real criticism of their effectiveness. It is reasonable personal and clinical philosophy for a couple to have *in vitro* fertilisation say two to four times in a year, which each time offers about a 25% chance of success compared with 3-4% by natural means during the intervals.

What is needed is a general raising of standards

of infertility practice to what is now undoubtedly achievable in all competent centres.

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- 1 Sheldon TA, Song F, Freemantle N. Assisted conception on the NHS. *BMJ* 1992;305:521. (29 August.)
- 2 *The management of subfertility*. Leeds. School of Public Health, Leeds University, 1992. (*Effective Health Care* bulletin No 3.)
- 3 Hull MGR. Infertility treatment: relative effectiveness of conventional and assisted conception methods. *Hum Reprod* 1992;7:785-96.

## Heterosexual AIDS epidemic

EDITOR.—Although the AIDS epidemic continues to grow and people are being infected worldwide, the medical literature trails behind. Almost half of the one million adults infected so far this year have been women. The gap in transmission rates in Britain and the rest of Europe between heterosexual and homosexual has narrowed. But information about the disease is still male dominated. At risk groups are still being highlighted, rather than high risk behaviour.

One general practitioner journal recently carried a whole symposium on HIV infection and AIDS and did not mention women once.<sup>1</sup> Another journal reviewed presentation and treatment of fungal infections in HIV without mentioning the vagina.<sup>2</sup> A recent atlas of AIDS showed out of 153 case presentations, only two presentations of women.<sup>3</sup> The list is endless.

Unless we challenge this women will continue to be diagnosed later, be given second class treatment, and forgotten when it comes to work on prevention.

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- 1 Symposium on HIV and AIDS. *Practitioner* 1991;235(May):409.
- 2 Mansfield S. How should fungal infections be treated in HIV patients. *MIMS Magazine* 1992 June 30:48.
- 3 Parkin JM, Peters BS. *Differential diagnosis in AIDS*. London: Wolfe, 1991.

## Low serum cholesterol and violent death

EDITOR.—Gunnar Lindberg and colleagues found that in men low cholesterol concentrations were associated with a higher rate of suicide in the subsequent six years.<sup>1</sup> Similarly, when Muldoon *et al* reviewed six trials of lowering serum cholesterol concentration by drug or diet they found a significant increase in deaths due to suicides and violence.<sup>2</sup> It seems possible that if a low cholesterol concentration predisposes a few to the extreme act of suicide then others are likely to experience less severe depression. The questions posed by these data may well be best investigated by using a more subtle measure than the rate of suicide. We reanalysed data on serum cholesterol concentration and mental health in a group of subjects.

Serum cholesterol concentrations in 130 men and 155 women (mean age 20.5 years) who had fasted overnight were related to scores on the general health questionnaire, which is designed to screen for psychiatric problems. The average cholesterol concentration was 4.03 (SD 0.73) mmol/l in the men and 4.47 (0.99) mmol/l in the women. The sample was grouped in terms of cholesterol values, and the scores on the general health questionnaire were analysed with analysis of variance; the interaction of sex and cholesterol concentration was significant ( $F_{2,268}=3.50$ ,  $p<0.03$ ). The table shows that there was no general relation between cholesterol concentrations

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.<sup>1</sup> 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, Råstam 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.<sup>1</sup> 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.<sup>2,3</sup> Loss of appetite and weight loss are characteristic of this state or illness,<sup>3,4</sup> and loss of over 5% of body weight is regarded as one of the diagnostic characteristics of acute depressive illness.<sup>3</sup> Weight loss is strongly associated with a fall in serum total cholesterol concentration.<sup>5,6</sup>

Among middle aged men 2.5-3.2% are estimated to have an acute depressive illness at any one time,<sup>3</sup> while others may suffer from reactive depression based on losses and social misfortune.<sup>2,4</sup> 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.<sup>2,3</sup>

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.<sup>2,3</sup> 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.<sup>7</sup>

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, Råstam 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.)
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- 3 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, third edition, revised*. Washington, DC: American Psychiatric Association, 1987.
- 4 Seligman MEP. *Helplessness: on depression, development and death*. San Francisco: W H Freeman, 1975.
- 5 Krombout 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, Råstam L. Serum sialic acid concentration and cardiovascular mortality. *BMJ* 1991;302:143-6.

EDITOR.—The paper by Gunnar Lindberg and colleagues provides support for a link between low serum cholesterol levels and suicide.<sup>1</sup> 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%<sup>2</sup> 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.<sup>3</sup>

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, Råstam 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.
- 3 Castellani WP, Doyle JT, Gordon T, Hames CG, Hjortland MC, Halley SB, et al. Alcohol and blood lipids. *Lancet* 1977;ii:153-5.

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.<sup>1</sup>

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.<sup>1</sup> The latest edition of the handbook on immunisation against infectious disease agrees with this and adds that the sites of injection should be recorded.<sup>2</sup> 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.<sup>1</sup>

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.