They note some of the properties of aprotinin including its antifibrinolytic and antiplasmin actions, and also the ability of plasmin and other enzymes to strip platelet glycoprotein Ib receptors. We suggest, however, that their conclusion that the efficacy of aprotinin in reducing blood loss after cardiac surgery shows the importance of fibrinolytic activation in perioperative bleeding may be invalid. The problem with this conclusion is that hyperfibrinolysis does not seem to be a major complication of modern cardiopulmonary bypass,^{2,3} though this is disputed by some. In addition, the observation that a single dose of aprotinin at the start of a bypass operation is as effective as a continuous infusion in reducing blood loss⁴ suggests that aprotinin's action against proteases such as plasmin, which are continually produced throughout bypass operations, cannot explain its prohaemostatic action. As the authors note, an acquired platelet defect has been incriminated as a major cause of non-surgical bleeding after cardiopulmonary bypass.

We suggest a previously unrecognised aetiology of this defect which may provide an explanation for the prohaemostatic action of aprotinin. This is based on unpublished work carried out at our unit with a new technique (haemostatometry) to assess platelet function.⁵ By using this method in 250 patients we have shown a wide individual variation in *in vitro* platelet inhibition with heparin at a dose equivalent to that given during cardiopulmonary bypass (about 30% showed severe inhibition). In 100 patients having cardiac surgery the group with severe *in vitro* platelet inhibition with heparin preoperatively had a significantly greater blood loss than those with moderate platelet inhibition. We also showed in 25 patients that the addition of aprotinin to heparin significantly reduced *in vitro* platelet inhibition, particularly in the group that had severe platelet inhibition with heparin alone.

We conclude that one of the modes of action of aprotinin in reducing blood loss after cardiac surgery may be by reducing the inhibitory effect of heparin on platelet function.

LINDSAY C H JOHN
GARETH M REES
IREN B KOVACS

Department of Thrombosis and Cardiothoracic Surgery,
St Bartholomew's Hospital,
London EC1A 7BE

- Hunt BJ, Yacoub M. Aprotinin and cardiac surgery. *BMJ* 1991;303:660-1. (21 September.)
- Royston D, Bidstrup BP, Taylor KM, Sapsford RN. Effect of aprotinin on need for blood transfusion after repeat open heart surgery. *Lancet* 1987;ii:1289-91.
- Harker LA, Malpass TW, Branson HE, Hessel EA, Slichter SJ. Mechanism of abnormal bleeding in patients undergoing cardiopulmonary bypass; acquired transient platelet dysfunction associated with selective alpha granule release. *Blood* 1980;56:824-34.
- Van Oeveren W, Harder MP, Roozendaal KJ, Eijssman L, Wildervuurt CRH. Aprotinin protects platelets against the initial effect of cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1990;99:788-97.
- Gorog P. A new, ideal technique to monitor thrombolytic therapy. *Angiology* 1986;37:99-105.

Unplanned pregnancies

SIR,—At last a head of steam is building up to do something about the problem of teenage pregnancies (and pregnancies among women in their early 20s).^{1,2} Unfortunately, we have lost 10 years because of the effective intimidation by a small fundamentalist minority who prefer to tolerate growing human misery than to live in the real world.

Ten years ago the Health Education Council commissioned the department of public health at Liverpool University to develop proposals for an intervention programme aimed at reducing unwanted and unplanned teenage pregnancy as well as sexually transmitted disease. A proposal was developed that took advantage of the remarkably

effective experience of the Dutch and the Swedes that entailed extensive consultation with community and religious leaders [details available from JA].³ That proposal was rejected for no good reason, but off the record briefings indicated clearly that it was rejected predominantly because the approach was not compatible with the fundamentalist fantasies of some of the government's influential advisers. Fortunately and somewhat dramatically, the climate has now changed completely. Government ministers are openly supporting planned parenthood initiatives against a background of large increases in the numbers of unwanted pregnancies. It should, however, be pointed out that such increases are compatible with teenagers as a group practising contraception more effectively than 20 years ago but may result from a higher proportion of new cohorts being sexually active at younger ages ($p=nsc$, where the number of pregnancies (p)=the number in the cohort (n) times their level of sexual activity (s) and their effective fertility (c), taking account of primary fertility and efficacy of contraception).

Unhelpfully, we are still in the dark about our national sexual behaviour because of the government's refusal to support the much needed research into this; fortunately, the rejected work that is now being carried out with funding from Wellcome should be available fairly soon and should provide a basis for us to get to grips with this major health problem. There can be little doubt that when we talk in the language of health gain and the cost effectiveness of services, family planning and planned parenthood are at the top of the list. This basic fact is reinforced by the findings of epidemiological work from Southampton, which indicate the importance of low birth weight with respect to risk of cardiovascular disease. What we should be doing is enabling women to have their one or two children at the time that is optimal for them and for their children's growth, development, and future health—or, as Margaret Mead put it, "What we need is not more but better quality children."

JOHN ASHTON

Department of Public Health,
Liverpool University,
PO Box 147,
Liverpool L69 3BX

- Pearson JF. Preventing unwanted pregnancies. *BMJ* 1991;303:598. (14 September.)
- Dillner L. Unplanned pregnancies. *BMJ* 1991;303:604. (14 September.)
- Ashton J. True story: the Liverpool project to reduce teenage pregnancy. *British Journal of Family Planning* 1989;15:46-51.

SIR,—In keeping with the view expressed in a previous editorial in the *BMJ* Mr James F Pearson suggests that the best way of preventing unwanted pregnancies in teenagers is to provide more comprehensive family planning services and sex education.² Although the argument is superficially plausible, it is not fully consistent with the facts.

The widespread availability and use of contraceptives among teenagers, in whom the failure rate is high, lead inevitably to an increase in unwanted pregnancies and a higher abortion rate. Figures from the Alan Guttmacher Institute for single women up to the age of 18 give a failure rate of 11% a year for the pill and of 18% for condoms and 32% for the diaphragm.³ The cumulative failure rate over five years rises to nearly 50% for the pill. As use of contraceptives has increased among teenagers so has the rate of unplanned pregnancies.⁴ Contraception in teenagers does not prevent unplanned pregnancies: used long enough it virtually assures them.

The most successful sex education programme in the United States, called Teen Star (sexuality teaching in the context of adult responsibility), uses experiential learning about fertility to help integrate biological maturity with understanding of the capacity for parenthood. Only after teenagers have come to terms with the fact that they are now

biologically capable of being a mother or father can they integrate awareness of this capacity into choices about present behaviour that are consistent with life goals.⁵ The results of this programme in 897 female subjects and 308 male subjects drawn from 20 teaching sites showed that sexual activity reduced significantly throughout the programme and for at least one year afterwards (H Klaus and D Kardatzke, meeting of Institute for International Studies in Natural Family Planning, Washington, DC, 10-13 December 1990). In contrast, a review of 33 sex education programmes in the United States found that contraceptive education resulted in gains in sexual knowledge but appreciable shifts towards promiscuity. One poll showed that after contraceptive education sexual activity in a school increased by half.⁶

The promoters of contraception and value free sex education sometimes admit that their policies are counterproductive.⁷ This may be because contraception dichotomises sex and procreation, thus facilitating fragmented relationships that do not lead to growth. The damage done to young people by mechanistic sex education devoid of any exhortation towards respect and responsibility has been truly devastating. It is worrying that there are still advocates of the very policies that increase teenage pregnancies. This is not what preventive medicine is meant to do.

GREGORY T GARDNER

Alvechurch,
Birmingham B48 7EA

- Smith T. Unwanted pregnancies. *BMJ* 1990;300:1154.
- Pearson JF. Preventing unwanted pregnancies. *BMJ* 1991;303:598. (14 September.)
- Grady W, Hayward M, Yagi J. Contraceptive failure in the United States: estimates for the 1982 national survey of family growth. *Fam Plann Perspect* 1986;18:204.
- Kiernan K, Wicks M. *Family change and future policy*. London: Family Policy Studies Centre, 1991.
- Klaus H, Martin JL. Recognition of ovulatory/anoovulatory cycle pattern in adolescents by mucus self detection. *J Adolesc Health Care* 1989;10:93-6.
- Richard D. *Has sex education failed our teenagers?* Pomona, Ca: Focus on the Family, 1990.
- Alan Guttmacher Institute. The effects of sex education on adolescent behaviour. *Fam Plann Perspect* 1986;18:162-9.

Abortion

SIR,—I always enjoy Professor James Owen Drife's contributions to the journal, but I wish that he had thought more carefully before dashing off his piece on induced abortion.¹ Although it is true that the British abortion rate is higher than the Dutch one, the rate in Scotland is one of the lowest in the developed world, and even in England and Wales the rate is only half that in the United States. Every effort should of course be made to prevent unwanted pregnancy, but exaggerating the problem is not helpful.

I am astonished that a sensitive gynaecologist with some experience of counselling women should have thought until now "that abortions happen to a little group of recidivists." Though there is limited evidence of some behavioural differences between women obtaining abortion and other groups, individual women seeking abortion are entitled to be treated as ordinary human beings and not stigmatised.

Lastly, I hope that any programme of education about sex and contraception will be offered to our sons as well as our daughters.

M H HALL

Aberdeen Maternity Hospital,
Aberdeen AB9 2ZA

- Drife JO. One in three. *BMJ* 1991;303:653. (14 September.)

SIR,—Professor James Owen Drife highlights the high termination rate in Britain of 15/1000 women aged 15-44 and then suggests that one in three women will have a termination in their lifetime.¹ Although I agree that our termination rate is

worryingly high, I think that the rate of one in three is misleading as it assumes a constant rate of termination throughout ages 15-44. This is not the case at present, as among women aged 35 and over the rate reduces to about 4 terminations per 1000 women. If the number of terminations is calculated on the basis of the three age groups 15-19, 20-34, and 35-44 it results in a rate of 200/1000 in the 30 years. This, when corrected for women who have had a termination previously, results in a figure of about one in six women having a termination in their lifetime.

PAT OWEN

Department of Public Health Medicine,
Cornwall and Isles of Scilly District Health Authority,
Truro TR1 1NR

1 Drife JO. One in three. *BMJ* 1991;303:653. (14 September.)

AUTHOR'S REPLY.—The abortion rates for older women have been fairly constant since 1969 at just over 7/1000 women aged 35-39 and 3/1000 women aged 40-44. These rates fell slightly in the late 1980s, possibly because nowadays almost half of British women over 35 have been sterilised or have a partner who has been sterilised.

Nevertheless, the annual abortion rate for women aged 16-24 is now 24/1000. Over this nine year period there is therefore an overall rate of 216/1000, which means that at least 1 in 5 women will have an abortion before the age of 25.

After I wrote my article I found a recent comprehensive review by Botting, of the medical statistics division of the Office of Population Censuses and Surveys, which included a calculation of the "projected average lifetime abortion rate."¹ Based on the rates in 1969-74, 28 women in every 100 would have an abortion at some time in their lives, whereas based on the rates for 1985-9 the figure rose to 42 in every 100. Therefore one in three may now be an underestimate, not an overestimate.

JAMES OWEN DRIFE

Department of Obstetrics and Gynaecology,
University of Leeds,
Leeds LS2 9NS

1 Botting B. Trends in abortion. *Population Trends* 1991;64:19-29.

Topical anaesthesia in upper gastrointestinal endoscopy

SIR,—We were pleased to see that Dr S Y Chuah and colleagues found that topical anaesthesia before upper gastrointestinal endoscopy was of no obvious benefit.¹ Although some potential hazards of premedication with lignocaine spray to the pharynx were mentioned (methaemoglobinemia, risk of aspiration, and damage to the ozone layer), we believe that the most serious potential hazard was not addressed.

Lignocaine is a powerful drug, and overdose can lead to depression of the cardiovascular, respiratory, and central nervous systems.² Peak blood concentrations of over 5 µg/ml—the level thought to give rise to toxic reactions—may occur after lignocaine has been applied to mucosal surfaces,^{3,4} and fatalities and severe reactions have been described after such administration.^{5,7}

Recent studies have shown significant episodes of hypoxia, arrhythmias, and myocardial ischaemia after upper gastrointestinal endoscopy.⁸ Such events are potentially aggravated by the concurrent administration of lignocaine.

Another potentially dangerous factor is that doctors have been shown to be unaware of basic information regarding the amount and maximum recommended doses of local anaesthetics.⁹ A recent survey that we carried out of 78 medical staff who regularly performed bladder catheterisation showed that all used lignocaine gel and yet only

one person was aware of how much he was administering.

As no obvious advantage was shown for the patient or practitioner by premedicating patients with lignocaine spray to the pharynx before upper gastrointestinal endoscopy, we believe that this practice, which may be an important factor in morbidity or mortality associated with such a procedure, should now be abandoned.

M T ALI

A W MURRAY

Department of Anaesthesia,
Newcastle General Hospital,
Newcastle upon Tyne NE4 6BE

S G TORDOFF

Department of Anaesthesia,
Leicester Royal Infirmary LE1 5WW

- 1 Chuah SY, Crowson CP, Dronfield MW. Topical anaesthesia in upper gastrointestinal endoscopy. *BMJ* 1991;303:695. (21 September.)
- 2 Rang HP, Dale MM. *Pharmacology*. Edinburgh: Churchill Livingstone, 1990:587.
- 3 Ouellette RD, Blute R, Jaffee S, Bahde C. Plasma concentrations of lidocaine resulting from instillation of lidocaine jelly into genitourinary tract prior to cystoscopy. *Urology* 1985;25:490-1.
- 4 Scott DB. "Maximum recommended doses" of local anaesthetic drugs. *Anaesthesia* 1989;63:373-4.
- 5 Adriani J, Campbell D. Fatalities following topical application of local anaesthetics to mucous membranes. *JAMA* 1956;162:1527-30.
- 6 Dix VW, Tressider GC. Collapse after use of lignocaine jelly for urethral anaesthesia. *Lancet* 1963;i:890.
- 7 Heath PK, Tometzki AJP, Gerrard DMP. Status epilepticus following rectal administration of lignocaine gel in a 2 month old baby. *BMJ* 1989;298:1592.
- 8 Murray AW, Morran CG, Kenny GNC, Macfarlane P, Anderson JR. Examination of cardiorespiratory changes during upper gastrointestinal endoscopy. *Anaesthesia* 1991;46:181-4.
- 9 Scrimshire JA. Safe use of lignocaine. *BMJ* 1989;298:1494.

SIR,—It is unfortunate that Dr S Y Chuah and colleagues' thoughtfully designed and long overdue investigation of the effectiveness of topical anaesthesia in upper gastrointestinal endoscopy will not prove useful in modern endoscopic practice¹: the mean dose of intravenous midazolam given is much larger than that now used by many, and probably most, endoscopists for straightforward upper gastrointestinal endoscopy and exceeds the usual range described in the data sheet.² The result of a repeat study in which about half the dose of midazolam was given would be valuable.

A F MACKLON

Shotley Bridge General Hospital,
Consett DH8 0NB

- 1 Chuah SY, Crowson CP, Dronfield MW. Topical anaesthesia in upper gastrointestinal endoscopy. *BMJ* 1991;303:695. (21 September.)
- 2 Association of the British Pharmaceutical Industry. *ABPI data sheet compendium*. London: DataPharm, 1990:1404.

Misuse of temazepam

SIR,—Professor D G Grahame-Smith recently gave a warning about misuse of temazepam,¹ and Messrs A N Meshikhes and J S Duthie reported erythematous swelling after injection of temazepam.² We report a case of severe rhabdomyolysis, oedema, and macular rash after misuse of temazepam.

A 28 year old woman presented four hours after attempting to inject into the right femoral artery 80 mg temazepam extracted from liquid filled capsules. She developed a purple macular rash, severe oedema, and exquisite tenderness of the whole of the right leg, which persisted for five days. Serum creatine kinase activity was 5900 IU/l (normal range 10 to 90 IU/l) and rose to 25 000 IU/l five days after the injection before falling to 311 IU/l 16 days after admission. She was treated with intravenous fluids to maintain a diuresis of 100 ml/h, and her renal function did not deteriorate, creatinine concentrations remaining normal throughout. She made a complete recovery.

In our case the early rise in creatine kinase activity indicated focal rhabdomyolysis. Although this phenomenon has been noted after an oral overdose of nitrazepam and doxepin,³ we believe this to be the first report of rhabdomyolysis after injection of temazepam.

An increasing number of addicts are misusing temazepam. Clinical awareness of the diverse manifestations of this and measurement of serum creatine kinase activity to detect rhabdomyolysis may help avert potentially severe side effects.

M M T HUDSON

M EDMONDS

P J WATKINS

Dulwich Hospital,
London SE22 8PT

- 1 Grahame-Smith DG. Misuse of temazepam. *BMJ* 1991;302:1210. (18 May.)
- 2 Meshikhes AN, Duthie JS. Misuse of temazepam. *BMJ* 1991;303:478. (24 August.)
- 3 Hojgaard AD, Andersen PT, Møller-Petersen J. Rhabdomyolysis and acute renal failure following an overdose of doxepin and nitrazepam. *Acta Med Scand* 1988;223:79-82.

Low cholesterol and coronary heart disease

SIR,—The conclusion of Dr Zhengming Chen and colleagues—and the title of the article, "Serum cholesterol concentration and coronary heart disease in population with low cholesterol concentrations"—misses a very important finding.

Notwithstanding their assertion that "there was no good evidence of an adverse effect of cholesterol on other causes of death," the researchers state in their results that "there was a significant inverse relation between serum cholesterol concentration and all deaths from non-vascular, non-cancer causes ($p < 0.05$)."¹ Moreover, all cause mortality (expressed as the ratio of observed to expected deaths) did not vary across the quartile groups of cholesterol concentration (1.1 in the lowest quartile to 0.97 in the highest)—in contrast to the impressive figures for differences in deaths from coronary disease.

In my experience people are interested in ways of reducing "all cause" mortality rather than of shifting the cause without affecting their lifespan; Dr Chen and colleagues' study adds to the large body of evidence that cholesterol concentration is not closely linked to overall mortality—and that a low cholesterol concentration merely makes death from a non-cardiac cause likely.

T H LEIGH

London SE21 8HS

- 1 Chen Z, Peto R, Collins R, McMahon S, Lu J, Li W. Serum cholesterol concentration and coronary heart disease in population with low cholesterol concentrations. *BMJ* 1991;303:276-82. (3 August.)

AUTHORS' REPLY.—Our study in an Asian population with low cholesterol concentrations indicates a strong positive relation between serum cholesterol concentration and deaths from coronary heart disease ($2p < 0.001$) with no evidence of any "threshold" within the range studied (about 3.8-4.7 mmol/l).¹ In Western populations the average cholesterol concentration is higher than that in Shanghai and few people have a concentration that is persistently as low as 4.7 mmol/l. This implies that very few people in Western populations have a biologically normal (as opposed to a laboratory "normal") cholesterol concentration and that for most of them a lower cholesterol concentration should eventually confer a lower risk of coronary heart disease.

To assess any causal relation between serum cholesterol concentration and total mortality, especially in a population in which only a small proportion of the deaths are due to coronary