Letters

Widow's attempt to use her dead husband's sperm

Twin pregnancy resulted in case that was similar but in which consent was obtained

EDITOR—The use of posthumous frozen sperm after chemotherapy is well established for patients with cancer although the success rate is low, but recent advances in intracytoplasmic sperm injection now offer a realistic chance of success. We describe a pregnancy in a widow after intracytoplasmic sperm injection with her dead husband's sperm and contrast this with the recent case in which another widow was refused permission to use her husband's sperm.

A childless widow was referred to us for treatment after her late husband's chemotherapy for testicular cancer was unsuccessful. Three ampoules of suboptimal sperm were frozen after written consent was obtained. Two ampoules were used for unsuccessful attempts at insemination, while the last was used for intracytoplasmic sperm injection. Three embryos were replaced, which resulted in a (continuing) twin pregnancy.

Sperm quality is adversely affected by testicular cancer and its treatment. This case shows that intracytoplasmic sperm injection with frozen sperm should be considered as an early treatment for a woman provided she fulfils the requirements of the Human Fertilisation and Embryology Authority. It also highlights the relative ease of obtaining legal consent in chronic terminal illness. By contrast, in the recent case the authority ruled that the lack of the husband's signed consent precluded the woman from using his sperm in Britain and elsewhere.[1]

Obtaining gametes for treatment without consent is permitted in exceptional circumstances in which treatment cannot be postponed and the patient is unconscious and cannot indicate his or her wishes (section 5.4, Human Fertilisation and Embryology Authority's code of practice). Ironically, storage of gametes without informed consent is forbidden (section 5.9b). Therefore, spermatozoa collected from an unconscious man cannot realistically ever be used for treatment in Britain unless he recovers. The authority has taken a similarly rigid stance in other issues, such as embryo freezing[2] and the withdrawal of payments to sperm donors,[3] and in a guide for patients wanting in vitro fertilisation.[4] If the widow's appeal is allowed it should not affect more than 0.001% of treatment cycles.[5]

As shown by our case, the Human Fertilisation and Embryology Authority is not opposed to posthumous assisted reproduction provided written consent is obtained. But death is seldom convenient. The comparison of the two cases shows the limitations of the current law: it is conveniently applicable in a chronic illness but not so in an acute illness. Such inflexibility is germane to neither the human condition nor a rapidly changing medical field.

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Widow is a victim of "corporate tyranny"

EDITOR—People banded together are capable of follies and excesses beyond what the same people, acting as individuals, would perpetrate on other individuals. Such activities, which may be termed "corporate tyranny," are marked by relative precepts being regarded as absolute commandments, what is seen as the public interest being preferred to individual welfare, and failure to distinguish between different degrees of misdemeanour.

I see an example of this in the recent refusal to allow a widow to use semen taken from her husband during his final illness, in an attempt to have the child that they both wanted.[1] The Human Fertilisation and Embryological Authority is of course legally correct and has the comfort of a High Court assurance to that effect. As the law stands, the woman's plea would require written consent from her husband; this could clearly not be obtained because he was already unconscious. There was, however, a statement from the widow that her husband had expressed the wish to have a child by her—not a particularly unlikely or contentious wish. The authority may have had grounds for not believing her, but, if so, these should have been made public. In the presumed absence of such grounds, the refusal seems a hard decision. It would surely have been possible to recognise in this case the impossibility of fulfilling the strict legal requirement and to allow the request. Instead, the authority has taken the further step of preventing the woman from taking the semen for use in a country where the procedure would not contravene the law.

It seems to me that this is a case in which the distress and hardship to an individual are glaringly obvious and the value to society, still less to any one person, minimal. That view presupposes that legal and ethical principles are contingent, and not absolutes that need to be defended at whatever cost to actual living people. Even statute law can be altered or repealed, given time; and common law is an organic growth of which we have some reason to be proud. It is even plainer that ethical principles are contingent on interpretation in the light of the existing situation. Medical ethical principles are made for people, primarily for patients, and not the other way round.

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1 Dyer C. Widow's case raises issues of informed consent. *BMJ* 1996;313:1351. (30 November.)

Serum cholesterol concentration and postpartum depression

Oestrogen may have been a confounder

EDITOR—Barbara Ploeckinger and colleagues use pregnancy and the puerperium as a model for investigating the possible link between falling serum cholesterol concentrations and low mood.[1] Although they controlled for progesterone concentrations, which seem to be lower in women with the maternity blues,[2] they make no mention of oestrogen concentrations. Oestrogen concentrations fall in the immediate puerperium, and clinical work has shown that oestrogen enhances mood[3]; indeed, a recent randomised placebo controlled trial showed that transdermal oestrogen is beneficial in postnatal depression.[4] This, coupled with menopausal data indicating that oestrogen

has a cholesterol lowering effect, indicates that oestrogen may have been a confounding variable in Ploeckinger and colleagues' study.

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Authors should read the literature that they cite

EDITOR—The importance of reading material before citing it has been much discussed. The short report by Barbara Ploeckinger and colleagues emphasises this.[1] This report, purporting to show an association between decreasing serum cholesterol concentrations and depression, cites a paper of which I was a coauthor as showing that serum cholesterol concentration is associated with suicide and violent deaths. The paper in fact showed no association between plasma cholesterol and violent deaths.[2] Indeed, a preliminary report, focusing exclusively on violent deaths, had been published[3] in response to the paper that initiated the concern about this issue.[4] In their comment Ploeckinger and colleagues cite the same paper as showing an association between serum cholesterol concentrations and behaviour and mood. There were no data on behaviour and mood in the paper in question.

In his commentary on Mahmoud Zureik and colleagues' paper on cholesterol and violent deaths Malcolm Law suggests that the production of a plethora of confusing reports can distract attention from the essential evidence.[5] Certainly the pressure to publish—stimulated by the research assessment exercise in Britain—means that researchers can spend too much time analysing data and writing reports and too little time reading. This contributes to the confusion that Law discusses. Thus papers fail to acknowledge or correctly interpret earlier data that may render them superfluous. Perhaps the increasingly formal letters that are required to accompany submitted papers could contain a declaration that an adequate literature search and review have been carried out and that literature that is cited has been read.

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Fifth of e antigen negative carriers of hepatitis B virus should not perform exposure prone procedures

EDITOR—Martyn Halle has reported on a surgeon with hepatitis B who transmitted the infection to a patient who subsequently died.[1 2] This case has put pressure on the Department of Health to review guidelines on the employment of healthcare workers with hepatitis B who carry out exposure prone procedures. The current guidelines exclude all carriers of hepatitis B virus who are also positive for hepatitis B e antigen (that is, those with high infectivity) from carrying out such procedures.

It has been recognised that carriers of hepatitis B virus who are negative for e antigen are occasionally the source of infection. These cases have been associated with the presence of the codon 28 precore mutation, which stops the synthesis of e antigen but still allows production of infectious virus. Many people will wish to know how common this mutation may be in our population. A cohort of over 300 carriers of hepatitis B virus who were representative of the general population of carriers (which includes healthcare workers) has been studied recently by several methods that assess infectivity: hybridisation and genome amplification of hepatitis B virus DNA and assessment of the presence of the precore mutation (table 1).

Our studies showed that 74 (88%) of the 84 carriers who were positive for e antigen and 18 (8%) of the 234 who were negative for e antigen had DNA by hybridisation. Seventy nine (94%) of those who were positive for e antigen and 89 (38%) of those who were negative for e antigen had DNA by genome amplification. When the point mutation assay was used in those with genomes that could be amplified, 47 carriers who were negative for e antigen—that is, 20% of all the carriers who were negative for e antigen—had a codon 28 mutation.

Studies in fulminant neonatal hepatitis have shown that transmission from mothers who are negative for hepatitis B e antigen can occur when hepatitis B DNA levels are very low or absent on hybridisation.[3] These cases have also been shown to be associated with the codon 28 precore mutation. Our genome amplification data show that roughly 2 in every 5 ((17 + 72)/(40 + 194) = 38%) carriers who are negative for e antigen may be potentially infectious, and this indicates that their participation in exposure prone procedures may have to be reviewed. If the presence of the precore mutant were used to identify potential infectivity then roughly 1 in 5 ((5 + 42)/(40 + 194) = 20%) healthcare workers who are negative for e antigen might be affected.

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Resuscitation witnessed by relatives

Has proved acceptable to doctors in paediatric cases

EDITOR—We are interested in the debate about whether relatives should be allowed to witness resuscitation attempts[1 2] and support the Resuscitation Council's recent guidelines.[3] For the past nine months our paediatric accident and emergency department has used a written protocol that designates senior and experienced nurses to be solely responsible for the relatives' needs when a child is undergoing resuscitation. Under this protocol, parents are invited to be present in the resuscitation room if they wish to be after they have been given a full explanation and after prior notification of the leader of the resuscitation team. Thus the first moments of the resuscitation are undertaken in the absence of the relatives, who are being informed by the designated nurse of the situation and the events they are likely to witness.

Table 1 Results of three methods used to assess infectivity in carriers of hepatitis B according to whether they were or were not positive for hepatitis B e antigen (HBeAg). Figures are numbers (percentages) of subjects

	Hepatitis B virus DNA			
HBe status	By hybridisation	By genome amplification	Codon 28 precore mutation	Total
Positive for HBeAg	74(88)	79(94)	0	84
Negative for HbeAg and antibody to HBe	4(10)	17(43)	5(13)	40
Positive for antibody to HBe	14 (7)	72(37)	42(22)	194
Total	92(29)	168(53)	47/234(20)	318

A recent poll of 27 doctors who are involved in paediatric resuscitation (nine consultants, five senior registrars, 13 registrars) showed that 23 had experience of a resuscitation witnessed by parents. Only three doctors thought that the experience for them had been negative (in two cases the parents had not been accompanied by an identified nurse, and in one the resuscitation had been prolonged unnecessarily because of the parents' presence).

The main themes arising included comments that doctors more experienced at resuscitation are more confident in allowing parents in the resuscitation room; parents should never be made to feel uncomfortable if they wish to leave (several parents had wished to remain with their child for only a few moments); and, essentially, an experienced, identified nurse should remain with the parents at all times, supporting them and explaining the events on behalf of the resuscitation team.

We would encourage emergency departments to develop the philosophy of inviting parents into resuscitation rooms if they wish to witness the resuscitation of their child as this does not hinder the resuscitation process. Emergency departments must have an identified, experienced member of staff whose sole responsibility is to the parents. Training in resuscitation and a coordinated resuscitation team are essential.

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Might lead to a complaint for breach of confidentiality

EDITOR—The Resuscitation Council has proposed that, under certain circumstances, relatives of adult patients should be permitted to witness resuscitation attempts[1]. We disagree with this proposal for two reasons.

Firstly, it is not possible simply to extend what is acceptable in paediatric practice to the care of adults. Whereas parents have legal responsibilities for the medical care of their children, in Britain relatives have no legal rights for the care of adult patients.[2] Doctors' primary duty is to patients, not relatives.

Secondly, the proposals ignore the requirements for patient confidentiality. Doctors are obliged not to disclose details of medical procedures to third parties without the patient's permission; those who breach this duty of confidentiality could find themselves the subject of disciplinary action.[3] Of course, patients will often ask doctors to share clinical details with a relative or friend, but for adults there is no automatic right to this, and doctors should obtain patients' permission before discussing their clinical condition with others.[2] Patients who are unconscious or gravely ill have the same rights to confidentiality as conscious patients, but it is, of course, impossible to obtain their views. In these circumstances doctors cannot assume that the patients would consent to their relatives witnessing their treatment. Indeed, between a quarter and a third of patients do not seem to want their relatives involved in decisions about whether resuscitation should be attempted,[4] so it seems unlikely that these patients would want their relatives to witness the actual procedure. Just because most patients die after resuscitation attempts (and are therefore not able to complain) we cannot assume that they would consent to their relatives witnessing their potentially degrading treatment.

Doctors should obviously try to deal with relatives of those being resuscitated in a sensitive and caring way, but we would caution them against inviting the relatives of adult patients to witness resuscitation. If patients survive they may have a strong case for complaint against their doctor for breach of confidentiality.

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Insulin infusion in diabetic patients with acute myocardial infarction

Effective components of care and patients who might benefit must be determined

EDITOR—Gail Davey and Paul McKeigue suggest that insulin infusion in patients with myocardial infarction is effective in those with known diabetes but may also benefit those with glucose intolerance.[1] This is not supported by a detailed analysis of a randomised trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (the DIGAMI study), to which the editorial refers.[2] In that study 1240 patients were randomised, and half were excluded because of inability or unwillingness to receive the intervention, which included a short term intravenous infusion followed by a multidose subcutaneous insulin regimen for at least three months.

Only patients at low risk who had not previously received insulin treatment benefited significantly, but whether all of these people had diabetes is uncertain as the study's definition of diabetes was either a prior diagnosis of diabetes or a blood glucose concentration of ≥11 mmol/l on admission (these latter patients were referred to as "previously unknown" patients in the study). Other studies have shown that such a definition will include patients with true previously undiagnosed diabetes (persisting hyperglycaemia, high haemoglobin A_1 concentration), patients with diabetes precipitated by the stress of infarction (persisting hyperglycaemia, normal haemoglobin A_1), and patients with stress hyperglycaemia who on follow up have normal or impaired glucose tolerance (transient hyperglycaemia, normal haemoglobin A_1).[3] Patients with stress hyperglycaemia have an increased mortality compared with subjects whose glucose tolerance remains normal,[3 4] and in the DIGAMI study there was an excess of the "previously unknown" patients in the control group. The increased mortality in the control group may therefore be partly explained by an excess of deaths in patients who did not have diabetes.

The authors of the study could not identify which component of the intervention was responsible for the reduced mortality at one year (the reduction in mortality in hospital and at three months was not significant). They excluded differences in cardiovascular treatment, although they did not provide any supporting data. Possible explanations included improved metabolic control at the time of infarction; improved cardiac function as a result of continuing insulin treatment; and general improvement in the care of the patients, which may have occurred at the same time as insulin treatment. A further explanation might be the withdrawal of sulphonylurea treatment, which the University Group Diabetes Program's study showed to have deleterious effects on cardiovascular mortality.[5]

Before this intervention package can be applied in routine clinical care further studies are necessary to identify the effective component and to determine which patients might benefit.

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Insulin should be continued for 12 months after acute event

Gail Davey and Paul McKeigue, in summarising the results of a randomised trial of insulin-glucose infusion followed by subcu-

taneous insulin in diabetic patients with acute myocardial infarction,[1] fail to emphasise an important aspect of the therapeutic implications of that study.[2] As they point out, the trialists randomised 620 patients with acute myocardial infarction and known diabetes (542) or hyperglycaemia on admission (78) to receive either an intravenous insulin infusion regimen or standard management in a coronary care unit. What careful reading of the study makes clear is that the protocol also required intensively treated patients to continue to receive four injections of subcutaneous insulin for at least three months. At discharge from hospital 87% of the infusion group and 43% of the control group were receiving insulin, while at one year the figures were 72% and 49%, respectively. In parallel, the glycated haemoglobin concentration remained approximately 0.7% lower in the infusion group throughout the follow up period. As Davey and McKeigue report, the main component of the reduction in mortality was an effect on deaths after the first three months. Thus in the infusion group there were 28 (versus 35) deaths before discharge, 38 (versus 49) by three months, and 57 (versus 82) by one year. Moreover, the reduction in mortality in the infusion group was maintained over a longer period of follow up (K Malmberg, personal communication).

The results of this study do not permit the benefits of insulin infusion in hospital to be distinguished from those of continuing insulin treatment for 12 months after the acute infarction. Similarly, the mechanisms of the benefit remain to be clarified, as these could be either a beneficial effect on damage to heart muscle as a consequence of improved metabolic control in hospital or a reduction in recurrent events, perhaps resulting from improved glycaemic control during the follow up period[3] or from the effects of insulin on the fibrinolytic system.[4] A new, and larger, study is currently being initiated in Scandinavia to explore these issues. In the meantime, however, diabetic and hyperglycaemic patients with myocardial infarction should be given insulin infusions for the acute event and should then receive subcutaneous insulin for at least 12 months thereafter.

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1 Malmberg K, Rydén L, Efendic S, Herlitz J, Nicol P, Waldenstrom A, *et al.* Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol* 1995;26:57-65.
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Authors' reply

EDITOR—B Miles Fisher is incorrect in stating that half of the randomised patients were excluded from the trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction. The authors of the study explain that although 1240 eligible patients were logged, randomisation did not occur until after exclusions were made. This may limit the generalisability of the findings of the study, but not the validity. We agree with Fisher that not all the patients were diabetic: it was for this reason that we raised the possibility of extending treatment previously reserved for patients with diabetes to those with hyperglycaemia but no diagnosis of diabetes.

Both John S Yudkin and Fisher raise the possibility that the reduction in mortality in the treatment arm could be attributed to better control of glycaemia by insulin treatment after discharge rather than to insulin infusion at admission. We agree that this possibility cannot be excluded, but differences in glycated haemoglobin concentrations between the intervention and control groups were small in relation to the effect on mortality. Although the main reduction was in mortality after discharge, this does not exclude the possibility that insulin infusion reduces mortality by preserving myocardial function. No trials apart from the study by the University Group Diabetes Program have suggested that sulphonylureas could have such a large effect on cardiovascular mortality.

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Disagreements still exist over the chronic fatigue syndrome

EDITOR—Although the ME Association welcomes the royal colleges' unequivocal conclusion that the chronic fatigue syndrome is a genuine and disabling condition,[1] we also agree that their report will "engender disagreement on both sides of the Atlantic."[2] We have no problem in accepting that the alternative name for the condition—myalgic encephalomyelitis (ME)—is pathologically incorrect, and this is a matter that we now intend to address. However, labels are important to patients as well as doctors, and support groups throughout the world are unanimous in their view that "chronic fatigue syndrome" is a totally inadequate way of describing the symptomatology and associated disability. The chronic fatigue syndrome may well become a dustbin diagnosis for anyone with chronic fatigue, and a new name that is acceptable to both doctors and patients clearly needs to be found.

On the subject of epidemiology, we believe that the prevalence figure given in the report—up to one million cases in primary care—is a gross overestimate, which cannot be justified on the basis of the small number of conflicting epidemiological studies. Such a figure is not reflected in claims for state sickness and disability benefits, and we have no knowledge of general practitioners with 20-40 patients with the chronic fatigue syndrome.

Our main disagreement with the report concerns its undue bias towards psychological explanations and treatments. Taking into account the fact that some studies have failed to concentrate on a strict definition of the chronic fatigue syndrome and that others have used questionnaires that "perform poorly as screeners for psychiatric morbidity in chronic fatigue syndrome,"[3] we cannot agree that the published literature can be used to justify the conclusion that about three quarters of patients have a coexistent psychiatric illness. Equally, we are surprised that no mention is made of the view that when depression coexists it is possibly a combination of neurobiological changes and the psychological distress that so commonly affects these patients.[4]

Our most stringent criticism is reserved for the section of the report concerning children, particularly the recommendation that "tuition at home should be reserved for the most severely affected," along with a clear implication that immediate return to school should be encouraged. Such advice will inevitably result in further conflict between parents, health professionals, and education authorities.

Many of these disagreements could have been resolved if the working party had consulted more widely during its preparation of the report. Sadly, an opportunity to create consensus has not materialised.

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Treating dysentery with metronidazole in Pakistan

EDITOR—Carine Ronsmans and colleagues' study of health professionals' knowledge of the treatment of dysentery in Bangladesh showed that less than half chose the correct treatment as recommended by the World Health Organisation in Bangladesh.[1] Metronidazole was chosen by 10.9-25.6% of the doctors and by 36.8-47.3% of the drug dispensers. Similar and worrying inappropriate prescribing practices for antiamoebic drugs have been reported recently in Pakistan.[2] In an editorial accompanying Ronsmans and colleagues' report Richard

Cash points out that inappropriate prescribing and dispensing might be explained by health professionals' dependence on drug companies for their information and medical education.[3]

The Medical Lobby for Appropriate Marketing (MaLAM) has recently questioned Rhône-Poulenc Rorer about its promotion for metronidazole (Flagyl) in Pakistan, which exhorts doctors to "Suspect amoebiasis/giardiasis in all cases of diarrhoea .... Immediate treatment is vital."[4] In its response Rhône-Poulenc Rorer endorsed that exhortation and stated that "If you agree that amoebiasis and giardiasis should be treated urgently due to their potential impact on morbidity and mortality, then empirical treatment [with metronidazole] becomes routine in a community unable to afford the charges for stool examination and other associated laboratory or office costs."

With respect, Rhône-Poulenc Rorer's assumption of amoebic hyperendemicity in childhood diarrhoea is not supported by the epidemiological evidence. Last year about 4500 children with acute diarrhoea were admitted to the King Edward Medical College and Mayo Hospital in Lahore. Only 80 (less than 2%) were found to be positive for giardiasis or amoebiasis.

Rhône-Poulenc Rorer's current promotion for the routine empirical use of metronidazole is in opposition to the WHO's recommendations, which state:

"Antiparasitic drugs should be used only for:

- amoebiasis, after antibiotic treatment of bloody diarrhoea for suspected shigella infection has failed or when trophozoites of *Entamoeba histolytica* containing red blood cells are seen in the faeces;
- giardiasis, when diarrhoea has lasted at least 14 days and cysts or trophozoites of *Giardia intestinalis* are seen in faeces or in the contents of the small intestine."[5]

Education programmes to change prescribing patterns for treating diarrhoea are needed. Any improvements, however, are unlikely to be sustained in the long term if health professionals and consumers remain exposed to prolonged drug promotion of this nature. Multinational drug companies promoting their products in developing countries are susceptible to the influence of international protest.[6] We invite the *BMJ*'s readers to support health professionals in Pakistan by expressing their concerns to Rhône-Poulenc Rorer about its recent promotion for metronidazole.

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Measurement error

A constant within subject standard deviation cannot be assumed a priori

EDITOR—In their statistical note about measurement error J Martin Bland and Douglas G Altman state that there is no point in estimating within subject standard deviation if we cannot assume that it is the same for all subjects.[1] This assumption, however, does not hold true in every clinically relevant situation. For example, the within subject standard deviation of many analyses is increased in patients from intensive care units. Even outside these extreme conditions, a constant within subject standard deviation cannot be assumed a priori. Homogeneity of within subject standard deviation must be verified before the estimate obtained from analysis of variance can be applied to determine whether two consecutive results in a single patient are truly different.[2]

When within subject standard deviation is not constant from one patient to another (presence of heterogeneity) the use of a single "mean" within subject standard deviation to estimate repeatability will underestimate the variability for several patients and will possibly lead to false conclusions about the clinical importance of the difference between two consecutive measurements made in these patients. In such cases the use of the 75th or 90th centile of within person variances across a population of similar patients has been suggested as a more appropriate estimate.[3]

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1 Bland JM, Altman DG. Measurement error. *BMJ* 1996;313:744. (21 September.)
2 Fraser CG, Harris EK. Generation and application of data on biological variation in clinical chemistry. *Crit Rev Clin Lab Sci* 1989;27:409-37.
3 Albert A, Harris EK. *Multivariate interpretation of clinical laboratory data.* New York: Dekker, 1987:207-41.

Author's reply

EDITOR—Jacques Massé raises a good point. There are several possible causes of heterogeneity in measurement error between subjects. One is that the measurement error may be related to the level of the measurement—for example, subjects with higher values of the measurement may have more variable repeated observations than subjects with low values. Typically, we find that the standard deviation of repeated observations in the same subject is proportional to the subject's overall mean. Altman and I have discussed this possibility and an appropriate analysis.[1]

It may also be that subjects in different populations have different within subject variations. A sample can tell us only about the population from which it is drawn, and when special populations such as those in intensive care are of interest it would make sense to sample them. We can then compare estimates of the within subject standard deviation between these populations. Finally, there may be heterogeneity between subjects which cannot be explained by a relation with the magnitude of the measurement. It seems to me that we should then try to explain this variation in terms of other subject variables (for example, obesity) if possible. If we cannot then I agree with Massé that a simple estimate of within subject variation could prove misleading. The method he suggests would be conservative—that is, tend to overestimate the measurement error for most patients—but this may well be preferable to underestimation.

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1 Bland JM, Altman DG. Measurement error proportional to the mean. *BMJ* 1996;313:106. (13 July.)

Measurement error is that which we have not yet explained

EDITOR—J Martin Bland and Douglas G Altman show how to calculate measurement error for repeated measurements, using as an example peak expiratory flow rates in a group of schoolchildren.[1] We wish to point out that some of what the authors describe as error can be identified, measured, and legitimately removed as a source of variation from the within subject error. The real measurement error is therefore lower than the authors have calculated. General and specific implications are sketched.

Observe that the mean measurement in the 20 children is 299.75 l/min when they are first measured but 305.25, 315.25, and 322 l/min in subsequent trials. Thus there seems to be evidence of an upward trend, which common sense suggests is a learning effect: over the four trials the children begin to get used to using the apparatus. Consequently, some of the variability in the measurements obtained for any particular child is due to something we should not really call measurement error, since we think that we know its origins.

Performing analysis of variance, as recommended by Bland and Altman, but now including the four trials as a within subject factor, we can partition the residual variance of 27 631 found in their table 2 into two components—namely, 5958 (due to a systematic difference between trials) and 21 673 (our new residual variance) (table 1). The F ratio associated with the "trials" shows that there are indeed significant differences in measured flow rates across the four trials, though it is beyond the scope of this letter to investigate further the precise statistical description of these differences. Our newly estimated standard deviation of the

Table 1 Analysis of variance for Bland and Altman's data

Source of variation	Degrees of freedom	Sum of squares	Mean square	Variance ratio (F)	Probability (P)
Children	19	285 318	15 017	—	
Trials	3	5958	1986	5.22	<0.01
Residual	57	21 673	380	—	

measurement error is 380.22 = 19.50 l/min rather than 21.5, as was previously calculated.

This example illustrates an important general point. Although the statistical notion of measurement error encourages the view of random, and therefore unknowable, deviations from a "true" reading, in practice so called error may often be systematic, quantifiable, and controllable. A more encouraging orientation is that measurement error is really that which we have not yet explained. The most immediate practical advantage of reducing unexplained variance/error is that it improves the resolution of the instrument of measurement. But chipping away at the as yet unexplained variance by showing how it arises also parallels the scientific process itself: that of making the unknown known by theory building.

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Dietary habits and mortality in vegetarians and health conscious people

Several uncertainties still exist

Editor—We believe that some of the issues raised in Timothy J A Key and colleagues' study of dietary habits and mortality in 11 000 vegetarians and health conscious people[1] and in the accompanying commentary by Matthew W Gillman[2] deserve more attention.

Firstly, the published literature on fruit and vegetables and cardiovascular disease is more extensive than Gillman suggests. When we reviewed the literature we located 10 ecological studies, three case-control studies, and 16 cohort studies reporting measures of association between intake of fruit and vegetables (or intake of nutrients mainly obtained from fruit and vegetables) and coronary heart disease, and we located five ecological studies, one case-control study, and eight cohort studies for stroke.[3]

Secondly, other cohorts at low risk have failed to show a protective association between intake of fruit and vegetables and cardiovascular disease (for example, a study of 26 473 Seventh Day Adventists followed up for six years showed null findings for fruit).[4]

Thirdly, while existing knowledge may endorse advice to eat more fruit and vegetables, clarification of areas of uncertainty that need further research remains important. What is the magnitude of benefit? Does it vary by level and source of background risk? Is there a threshold? Is seasonal variation important? Are some fruits and vegetables more protective than others? Do the fruit and vegetables have to be fresh?

Reporting of cohort studies of diet and chronic disease needs to be improved. Null findings have been inadequately reported. Food based analyses should be reported alongside analyses of specific constituents, whether nutrients or non-nutrients. Inconsistencies in findings between studies and populations should provoke further inquiry.

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1 Key TJA, Thorogood M, Appleby PN, Burr ML. Dietary habits and mortality in 11 000 vegetarians and health conscious people: results of a 17 year follow up. *BMJ* 1996;313:775-9. (28 September.)
2 Gillman MW. Enjoy your fruits and vegetables. *BMJ* 1996;313:765-6. (28 September.)
3 Ness AR, Powles JW. Fruit and vegetables and cardiovascular disease: a review. *Int J Epidemiol* (in press).
4 Fraser GE, Sabate J, Beeson WL, Stahan TM. A possible protective effect of nut consumption on risk of coronary heart disease: the Adventist health study. *Arch Intern Med* 1992;152:1416-24.

Weight cannot be interpreted without information on height

Editor—Timothy J A Key and colleagues explore dietary influences on mortality and, among important negative findings, note "no significant association between weight and mortality," which they qualify as "perhaps [being] because of the low numbers of obese subjects."[1] The original questionnaire, however, did not address height, and weight cannot be interpreted without information on height. In fact, the authors cannot comment on the numbers of obese or underweight subjects in their sample without such information, nor can they assume that the heights of their sample would approximate to those of a comparable sample of non-health conscious omnivorous subjects. By dividing their sample into thirds of weight distribution and calculating mortality ratios accordingly they miss the point that the group making up the middle third may contain an appreciable number of subjects with a higher body mass index than that in the top third.

Furthermore, questionnaire studies are notoriously inaccurate in delineating subjects with eating disorders and particularly anorexia nervosa, given its egosyntonic nature. Anorexia nervosa carries a mortality as high as 18.1% on 20 year follow up,[2] with most deaths being attributed to medical complications rather than suicides.[2] The study assumes that subjects record their dietary consumption accurately.

Such comprehensive studies have a tendency to be translated into policy in the longer term—for example, in the strategies of the Health of the Nation policy—and therefore it is important to recognise the flaws as well as the strengths.

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1 Key TJA, Thorogood M, Appleby PN, Burr ML. Dietary habits and mortality in 11 000 vegetarians and health conscious people: results of a 17 year follow up. *BMJ* 1996;313:775-9. (28 September.)
2 Theander S. Research on outcome and prognosis of anorexia nervosa and some results from a Swedish long term study. *Int J Eat Disord* 1983;2:167-74.

Authors' reply

Editor—We agree with A R Ness and J W Powles that many uncertainties remain concerning the relations between consumption of fruit and vegetables and the risk of cardiovascular disease. Their review is a valuable assessment of the evidence to date.[1] We hope that large cohort studies currently under way will answer many of the outstanding questions they pose.

John Farnill Morgan points out that, in the absence of information on height, we used weight as a crude index of obesity. Weight was positively associated with mortality from ischaemic heart disease as expected, with a rate ratio of 1.28 (95% confidence interval 0.97 to 1.69) in the top third relative to the lowest third of the weight distribution. We did not intend that this should be interpreted as a negative finding. Body mass index is certainly better than weight as a measure of obesity, but the correlation between these two variables is strong, and in nutritional epidemiological studies weight is probably a much better measure of obesity than the dietary variables are a measure of actual dietary intakes. For example, in the Oxford vegetarian study (a cohort of roughly 11 000 men and women comparable to those in the health food shoppers study) the correlation of weight with body mass index is 0.82, weight correctly classifies 65.0% of men and women into thirds of body mass index, and misclassification to the extreme thirds is only 2.4% (unpublished data). We estimate that this degree of random misclassification would cause underestimation of risks such that an observed risk of 1.3 for the top third of weight relative to the lowest third would represent a risk of approximately 1.5 for the top third of body mass index relative to the lowest third. Thus, while weight is an imperfect measure of obesity, we think that the results for weight provide useful information provided that they are interpreted carefully.

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1 Ness AR, Powles JW. Fruit and vegetables and cardiovascular disease: a review. *Int J Epidemiol* (in press).

Safeguards are needed for new proposals for primary care

EDITOR—Opportunity and threat are inextricably linked. Mike Pringle sees the government's last but one white paper as the opportunity for a thousand flowers to bloom.[1 2] We see it as a threat to the survival of general practice, particularly in deprived inner city areas. It makes no attempt to address the reasons for the crisis in the recruitment, retention, and morale of inner city general practitioners—namely, poor premises, frozen improvement grants and staffing budgets, inadequate support services for patients with mental illness or drug or alcohol problems, and lower than average net remuneration combined with above average workloads.[3] It ignores the existing strengths and commitment of both large and small inner city general practices and instead offers this government's stock panacea—deregulation—with no regard to the cost in terms of equity, social cohesion, and continuity of personal care.

A possible scenario goes as follows. Many singlehanded vacancies will arise in inner city areas in the next few years as a generation of doctors (largely from overseas), who have been the backbone of inner city practice since the 1960s, move into retirement. A shortage of applicants, combined with the proposed requirement that they should be able to meet the standards set out in whatever job description a health authority decides on, could ensure that many of these vacancies remain unfilled. This will then provide the opportunity—even the necessity—for pilot trials by health authorities. These are likely to include the employment of salaried general practitioners by NHS trusts and a variety of commercial organisations, including high street pharmacy chains and supermarkets. Contracts imposed on these general practitioners could include the kind of "gagging" clauses that are common for the existing employees of trusts, and also the imposition of limited formularies and referral rights, amounting to a severe curtailment of clinical freedom. Doctors taking up these posts are likely to be relatively inexperienced or from overseas and therefore less able to resist the imposition of such contracts. The recruitment of doctors into such posts would also undermine the ability of existing partnerships to recruit replacement or additional doctors, exacerbating stress related to workload and adversely affecting the care available to patients.

Protestations of good intent and reassurances that choice will remain with the profession are not enough. Real safeguards are needed. These are not to be found in the white paper, and if they do not appear in the bill they will need to be fought for during its passage through parliament.

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1 Pringle M. Primary care: choice and opportunity. *BMJ* 1996;313:1026-7.
2 Secretary of State for Health. *Primary care: the future. Choice and opportunity.* London: HMSO, 1996.
3 Lorentzon M, Jarman B, Bajekal M. *Report of the inner city task force of the Royal College of General Practitioners.* London: Royal College of General Practitioners, 1996. (Occasional paper 66.)

Information shared in mentoring must remain confidential

EDITOR—While Robert Alliott makes passing mention of mentoring schemes in several regions in his article in Career Focus,[1] he does not acknowledge the evident and specific influence on his own study of the pioneering three year mentor project in South Thames, which is currently being evaluated. A particularly relevant finding from this evaluation is the link between effective outcomes of mentoring interventions and the mentee's reliance on the confidentiality of information shared with the mentor. Alliott's suggested extended use of such privileged information, even if anonymous, suggests the concurrent pursuit of institutional objectives, which would risk distortion and diminution of the reason for the existence of mentoring support and, on the basis of our experience in South Thames, would be hard to justify.

Mentoring is well established in other professions as a means of professional development,[2] and the literature points to inherent tensions in the role of the mentor if he or she also contributes, at whatever distance, to an assessment of performance at work.[3] Feedback on performance is, of course, essential for professional development,[4] and the mentor is poised to provide it, but only if certain criteria are met.

The evaluation in South Thames shows that the unbiased and neutral role of the mentor, with the crucial absence of any "report back" function, is a critical factor in the mentee's ability to confront problems relating to organisational and clinical management and to work confidently towards achieving positive and effective change. All 65 mentees who were questioned attached appreciable value to the absolute confidentiality of their discussions with their mentor. Indeed, anxieties about how privileged information from the mentor interview might be used led to debates about what link (if any) might develop between, for example, mentoring and recertification.

The Anglia project discussed by Alliott provides further evidence of the potential of mentoring in reducing job related stress. South Thames can go further, with indicators that suggest that organisational issues such as morale and retention of practitioners can thereby also be addressed. Our experience, however, leads us to judge that use of information voiced in individual mentoring sessions to help resolve wider organisational issues, by another institutional route, will critically undermine the foundation on which our model of mentoring for promoting continuing medical education and professional development is essentially based.

The author's suggestion that local medical committees and the General Medical Council could make constructive use of this source of information puts confidentiality at risk. This must be strictly adhered to if the essential principles of mentoring are to be upheld.

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1 Alliott R. Facilitatory mentoring in general practice. *BMJ* 1996;classified suppl:Sep 28. (http://www.bmj.com/bmj/classified/7060cf.htm)
2 Merriam S. Mentors and proteges: a critical review of the literature. *Adult Education Quarterly* 1983;33:161-73.
3 Shaw R. Can mentoring raise achievement in schools? In: Wilkin M, ed. *Mentoring in schools.* London: Kogan Page, 1983:10-1.
4 O'Hanlon C. The importance of an articulated personal theory of professional development. In: Elliott J, ed. *Reconstructing teacher education.* London: Falmer, 1993:23-4.

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