Letters

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Doctors must learn to let others treat them and their families

Editor—My parents, who are 92 and 86 and otherwise in excellent health, are both virtually blind as a result of glaucoma detected too late. It is not their having the condition that saddens me, as they still manage to maintain their independence and constantly push the boundaries of their impairment in order to enjoy life to the full. What is sad is that neither of them can attribute late diagnosis and the attendant complications to social deprivation, poor access to medical care, or any of the factors identified by Fraser et al.[1]

Quite the opposite, in fact. My father is a retired general practitioner, a prominent member of the community in which I grew up. The best ophthalmologists in town would have readily investigated and treated him or any of his immediate family free of charge—if they had been asked to do so.

The problem is that too many doctors still tend to treat themselves and their families rather than delegate this important responsibility to colleagues. In doing so, they sacrifice objectivity and sentence themselves and their families to a lifetime of well meant, but severely compromised, medical care. My father was no exception.

How many doctors are able to separate their personal and professional responsibilities and enter themselves and their families into appropriate health surveillance programmes, so that conditions such as glaucoma are not missed? The alternative—seeing your children die of diseases associated with social deprivation and poor access to medical care—is sobering.

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1 Fraser S, Bunce C, Wormald R, Brunner E. Deprivation and late presentation of glaucoma: case-control study. *BMJ* 2001;322:639-43. (17 March.)

Advice to authors

We prefer to receive all responses electronically, sent directly to our website. Processing your letter will be delayed unless it arrives in an electronic form.

We are now posting all direct submissions to our website within 24 hours of receipt and our intention is to post all other electronic submissions there as well. All responses will be eligible for publication in the paper journal.

Responses should be under 400 words and relate to articles published in the preceding month. They should include ⩽5 references, in the Vancouver style, including one to the BMJ article to which they relate. We welcome illustrations.

Please supply each author's current appointment and full address, and a phone or fax number or email address for the corresponding author. We ask authors to declare any competing interest. Please send a stamped addressed envelope if you would like to know whether your letter has been accepted or rejected.

Letters will be edited and may be shortened.

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Recommendations for suspended doctors must be enacted

Editor—As the wife of a suspended doctor, I am well placed to comment on issues raised in the anonymous Personal View by the daughter of a doctor who had been suspended.[1] My family's lives have been turned upside down. I concede that every adverse incident must be thoroughly investigated, but it is the method by which it is done that fails the profession.

My husband has been subject to the most harrowing of press invasion, having been stalked so that "that photo" could be shot. There are front page headlines in the local newspaper after reporters have invaded our privacy at times when most people are off duty, weekends and evenings being favourite. The reporters tell us with apparent glee how our life is to unfold, having information that, as we have not yet been told it, can come only from a trust leak.

The result of this is a very depressed man—no longer the happy, hard working doctor who dedicated his adult life to medicine but a psychological shadow of his former self, someone who is now an exhausted recluse, unable to sleep, unable to function. A husband who is no longer my rock but another irksome child. A father who no longer bounces children on his knee, but a man more at one with the plants in the greenhouse.

Retraining is thought to be the answer. If it is so, then it has to be swift before the relationship between the trust and the doctor breaks down irreversibly and the doctor loses the desire to return to medicine and the trust becomes so wrapped in the desire to apportion blame that the whole situation becomes adversarial.

Once the investigation is over, and should retraining be the recommendation, then this should be compulsory on both sides. No doctor should have retraining recommended, only for the trust to decide on dismissal. This makes a mockery of the whole process.

The General Medical Council is on a death march, killing as it dies itself. I urge doctors, as professionals, to take action: they pay for the council, after all. It is strange that today, more than ever before, they are likely to be struck off by the council and yet they pay increasingly more for that privilege.

Ironically, the only winners in all this are the lawyers. They seem to be getting rich on the back of doctors' misfortune.

1 When a doctor is suspended so is family life. *BMJ* 2001;322:683. (17 March.)

Closing the gap between professional teaching and practice

Applying ethical principles is sometimes difficult for students

Editor—In raising points regarding the ethics of the provision of clinical education, Doyal suggests a framework to guide both teachers and students when interacting with patients clinically.[1] On numerous occasions I have been placed in uncomfortable positions where I have felt conflict between my ethics (for example, being asked to undertake femoral arterial blood gas analysis on a comatose elderly patient without any consent having been obtained from relatives (I refused)) and my natural desire to acquire clinical skills.

Students walk this ethical tightrope every day; to refuse to do something or to object one has to tread carefully. It is often the same clinicians who put the student in this difficult position who are assessing him or her for the final grade on the clinical attachment. The move towards continuous assessment rather than a final examination has meant that students are under even greater pressure to conform during their attachment.

Returning to medical school after undertaking postdoctoral research work and teaching some students myself, I have been

amazed by the deference expected of students towards the "authority" of clinicians who teach us. We are often expected only to answer, not to ask questions or provoke ethical debate. In some cases one must assume a serf-like acceptance that the clinician is always right, even when clear ethical boundaries are breached.

I have tried—not always successfully and not without some risk of incurring the wrath of a teacher—to maintain my ethical beliefs. Sadly, the application of ethical principles by students is difficult in practice because as students we experience little respect from a profession steeped in the expectation of students conforming and in the belief that teacher knows best. Not to conform can invite failure.

"Success" (a high grade) in clinical attachments is often best attained by students who apply ethics selectively—those who pay lip service to the theory of ethics but if put in an ethically dubious position by arrogant teachers do not question, do not rock the boat, and "do as they say to secure that grade A." My experiences lead me to believe that the educational system in medicine rewards those students who are more likely as doctors to develop into arrogant clinicians, indifferent to ethical responsibility to patients, who perpetuate the errors that haunt the profession today.

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Ethical guidance for teaching applies to postgraduate education as well

EDITOR—Doyal's guidelines on the ethics of medical education initially seem to apply only to undergraduate students.[1] However, all doctors in training face similar ethical dilemmas, and we would commend elements of the guidelines to organisations responsible for educating postgraduate doctors.

The issues of verbal consent to present cases and examination under anaesthesia apply to all training grades. We would propose one further addition to the guidelines, which relates to the teacher's attitude to both the learner and the patient. Guidance for postgraduate doctors, extracted from the paper by Doyal with the additional guideline, could read as follows:

- Clinical teachers and doctors in training should not perform physical examinations or present cases that are potentially embarrassing for purely educational purposes without the patient's verbal consent (including to the number of doctors present)
- Doctors in training should not perform any physical examination for purely educational purposes on patients under general anaesthesia without the patient's prior written consent, which should be placed in the notes
- Education should not be demeaning to the patient or doctor. The patient should be involved as a partner, and the doctor in training should be treated as an equal colleague
- Doctors in training should introduce themselves and explain their role as fully qualified doctors gaining additional experience in one specialty
- Clinical teachers are responsible for ensuring that these guidelines are followed. If doctors are asked by anyone to do anything to the contrary they should politely refuse, referring to these guidelines.

Most patients agree to participate in education, although the proportion is lower for internal or intimate problems.[2] Guidance helps remind clinical teachers about expected standards and provides a resource for doctors in training to help them in their discussions with clinical teachers of all specialties, including general practice.

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2 O'Flynn N, Spencer J, Jones R. Consent and confidentiality in teaching in general practice: a survey of patients' views on presence of students. *BMJ* 1997;315:1142.

Spreading research in primary care safely

EDITOR—The contributions by Green and Dovey and Thomas et al discuss general practice research networks. They highlight how crucial research based in primary health care is to the effective delivery of this care and the understanding of population health.[1 2] The news section of the same issue, however, reports the suspension of an east London general practitioner for entering patients in a trial without consent and forging signatures.[3]

I am concerned about how the potential of general practices to contribute to research, whether it be experimental or observational, can be maximised, while the registered patients and primary healthcare team can be supported in ensuring that research is safe and worthwhile. This needs to be discussed in terms of facilitation and funding, and through governance procedures for all practices and community health settings.

Currently the pharmaceutical industry and other outside agencies, including hospital academic departments, make regular approaches, in the case of the first, to practices to provide data or enter patients into studies. The practice team is often unsupported in judging the appropriateness and, when primary care is underfunded, may be swayed by inducements. At the same time, in practices, new investigators, perhaps considering extending audit or doing a project as part of continuing professional development, may be unaware of the possible ethical and practical pitfalls.

The Department of Health and the Royal College of General Practitioners are rolling out, after a pilot study, an elaborate accreditation procedure for research practices at two levels, collaborative and independent, which is to be priced at £2600, in addition to considerable cost to the practices in time and effort. Accreditation may soon become a requirement for research funding. There are no clear guidelines about what makes a good and safe research practice, other than an extensive list of criteria reviewed for accreditation and practices have to be already involved in research to be accredited. Such a procedure in its present form would only ever involve very few practices.

It is right in giving large grants to support research to aim to ensure the safe and effective use of them, and the accreditation of organisations managing them is probably very appropriate. How does this fit in, however, with maximising the potential of general practice to provide that laboratory for population research in terms of appropriately accessing participants or supporting primary care team members as developing researchers? Does there not need to be a much more basic and practical framework for governing and facilitating general practices in relation to research, which could have avoided the situation in east London?

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Competing interests: AEL is a member of East London and Essex Network of Research Practices.

1 Green LA, Dovey SM. Practice based primary care research networks. *BMJ* 2001;322:567-8. (10 March.)
2 Thomas P, Griffiths F, Kai J, O'Dwyer A. Networks for research in primary health care. *BMJ* 2001;322:588-90. (10 March.)
3 In brief. *BMJ* 2001;322:572. (10 March.)

Consumers are helping to prioritise research

EDITOR—We welcome the increasing participation of consumers in designing, conducting, and interpreting the results of randomised controlled trials.[1] At the National Coordinating Centre for Health Technology Assessment we also recognise the importance of asking consumers to help decide which trials are needed.

The health technology assessment programme aims at ensuring that high quality research information on the costs, effectiveness, and broader impact of health technologies is produced in the most efficient way for those who use, manage, and provide care in the NHS. People from all these groups have helped determine priorities for the programme.

Widespread consultation identifies up to 1500 suggestions a year. These are prioritised by expert panels, aided by short scientific summaries of possible research (vignettes) written by staff of the national centre with the help of experts in the field. Researchers are then commissioned, following peer review, to produce health technol-

ogy assessments, which are published—again after full peer review—as a health technology assessment monograph. Consumers were formally introduced into this process in 1997 and are now engaged throughout the process.

For each task we have developed job descriptions and person specifications and established procedures for identifying consumers and inviting and supporting their participation. When giving their views on research vignettes consumers are asked to comment on the importance of the research question, the tone and flavour of the vignette, and changes or additional information that would be useful. Consumer referees of research proposals are particularly asked to consider the choice of outcomes, patients' views about health care and needs for information and support, and patients' relevant experiences in healthcare settings and everyday life.

Consumers refereeing research reports provided positive, reassuring comments and suggested changes. Some raised issues not previously mentioned and gave useful opinions on the ranking of recommendations for research. Some gave sensitive interpretations of the results from the consumer perspective, with suggestions on how the report might be made more accessible and informative. Occasionally, some were critical—for example, questioning how outcomes are measured.

Feedback has been invited from consumers and those working with them. Key developments in response to this feedback have included establishing a mentor scheme for new members of the consumer panel, amending guidelines and forms for referees to make them more consumer friendly, and training staff of the national centre to seek out and support consumer expertise. Further details are available by post[2] and at www.ncchta.org.

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2 Oliver S, Milne R, Bradburn J, Buchanan P, Kerridge L, Walley T, et al. Involving consumers in a needs-led research programme: a pilot project. *Health Expectations* 2001;4: 18-28.

Is bigger better for primary care groups and trusts?

Small can be beautiful and effective

Editor—Bojke et al highlight the importance of deciding the optimal size of primary care organisations.[1] Their article reinforces my view that if these organisations are to fulfil their potential then false economies of scale must not be the main driving factor, as they have been with so many NHS reorganisations in the past.

For once the development of an NHS organisation should be based on its key roles and the environment in which it works to enable it to be as responsive as possible. This is especially the case for primary care organisations. It would be a disaster for primary care and local services if these organisations became reincarnations of health authorities or developed into the inflexible hierarchical institutions that are hospital trusts.

To Bojke et al's conceptual framework I would add the question "What type of organisation is needed to deliver the potential of a primary care trust?" The tasks faced require our organisations to be flexible, dynamic, supportive, enabling, and learning organisations. The organisations also require ownership from the people on the ground and time to develop before we move headlong into another straitjacketed, bureaucratic institution.

We shouldn't let a good concept get lost in political short termism or false economies of scale and risk losing the considerable gains so far. Small can be both beautiful and effective.

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Culture and leadership are also important

Editor—Bojke et al discuss the positive and negative aspects of larger primary care trusts.[1] Rapid responses to the article on bmj.com have pointed out that, despite the concept that greater size equals greater equality, larger primary care trusts do not necessarily deliver better health care.[2]

As Bojke et al suggest, the increased size of a primary care trust (through merger) does not guarantee greater efficiencies and effectiveness—in fact, quite often the opposite is true. The larger the organisation the greater the bureaucracy and the greater the remoteness from customers (patients). Indeed, many of the researchers into mergers have concluded, in the commercial sector at least, that under two fifths of mergers are successful.

Organisational, cultural, and leadership issues are important. Healthcare organisations are similar to many other businesses in the way in which they develop identities and are led. Many mergers have failed because the new organisation was unable to absorb the previous organisations successfully. Pressures by health authorities and others to merge unwilling and often quite different primary care groups into one primary care trust are, in my opinion, doomed to failure. Cultural clashes, divided loyalties, and lowered staff morale will not yield the benefits and equalities for which some people yearn.

The real focus should be on the delivery of primary health care in the most local and effective way possible while exploring the benefits of efficiencies through wider shared services arrangements.

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2 Electronic responses. Is bigger better for primary care groups and trusts? bmj.com 2001;322 (www.bmj.com/cgi/eletters/322/7286/599; accessed 28 June 2001).

Larger trusts may reduce inequalities

Editor—Bojke et al highlight the debate taking place as primary care groups realise that they will have to merge to be able to cope with the increasing agenda being set by central government.[1] As primary care trusts get larger it is imperative that an equal emphasis is placed on developing and empowering smaller localities within the trust.

The authors fail to examine one of the main reasons why mergers of primary care groups and trusts should be encouraged, particularly in cities. In many large towns and cities several primary care groups have been created where once only one health authority covered the area. This increase in independent organisations has meant that, rather than historical inequalities in the provision of health care being addressed, the differences between areas are increasing. What postcode you have is becoming the main determinant of the standard of health care you receive.

The best way to avoid increasing inequalities in primary care is to ensure that as few organisations exist as possible.

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Elderly people's technique in using dry powder inhalers

New inhaler devices are rarely used by older people in the community

Editor—Diggory et al report on the inhaler technique of older adults using two dry powder devices, the Diskhaler and Turbohaler; they had not used an inhaler before.[1] Greater competence was found with the Turbohaler. This device was also shown to be superior in an earlier study when it was compared with a pressurised metered dose inhaler attached to a spacer device.[2]

Satisfactory inhaler technique is influenced by cognitive function. As more recently developed devices require fewer steps before lung inhalation, and inspiration and actuation may not require simultaneous

coordination, theoretical advantages exist for older patients with cognitive impairment.

We have investigated use of different inhaler devices and technique in elderly people living in the community. A stratified random sampling method was used to select 6000 adults aged ≥65 years from 21 general practices in north Bristol. Each subject was sent a respiratory questionnaire in 1997. Altogether 4792 (80%) responded, with 662 indicating use of inhalers.[3] We then randomly selected 556 from those reporting any treatment for airways disease (n=708) for investigation in 1998-2000. The type of device(s) was recorded and technique assessed with a standardised approach.[4]

Altogether 244 subjects participated (mean age 74 (range 65-96)); 185 declined, 81 had died since completing the questionnaire, 38 had moved, and 8 were too unwell for study. Of those seen, 221 were using an inhaler. Ninety eight used a pressurised metered dose inhaler with a spacer, 81 used a pressurised metered dose inhaler without a spacer, 8 used a breath actuated device, 8 used dry powder devices, and 26 used combinations of these including nebulisers. Only five subjects were using a Turbohaler to deliver some or all of their inhaled treatment.

Unsatisfactory technique was found in 53% (43/81) using a pressurised metered dose inhaler alone, 32% (31/98) using a pressurised metered dose inhaler with a spacer alone, 50% (4/8) using a breath actuated device alone, 38% (3/8) using dry powder devices alone, and 46% (12/26) using combinations. Failure to shake the device, poor coordination of actuation and inhalation, and absence of breath holding were the commonest errors.

Despite favourable findings supporting the use of newer devices, they were rarely used in our population of older people. Factors influencing choice of inhaler are unclear, but cost is probably a major issue. From the perspective of the prescriber, there are insufficient comparative data on the relation between optimising inhaler technique through use of different devices and disease control and use of health care over time.

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Competing interests: The authors have received educational grants from 3M, MSD, Boehringer Ingelheim, and GlaxoWellcome supporting attendance at respiratory meetings. This study was funded by the NHS Research and Development programme in asthma care.

1 Diggory P, Fernandez C, Humphrey A, Jones V, Murphy M. Comparison of elderly people's technique in using two dry powder inhalers to deliver zanamivir: randomised controlled trial. *BMJ* 2001;322:577-9. (10 March.)
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3 Dow L, Phelps L, Fowler L, Waters K, Coggon D, Holgate ST. Respiratory symptoms in older people and use of domestic gas appliances. *Thorax* 1999;54:1104-6.
4 National Asthma and Respiratory Training Centre. *Guidelines for inhaler technique, diploma in asthma care*. 8th ed. Stratford upon Avon: Stratford Repro, 1998.

Zanamivir and unreason seem to go together

Editor—Zanamivir's effect on flu is disputed, but there's no doubt about its capacity—or, rather, the idea of its capacity—to paralyse logic. The National Institute for Clinical Excellence (NICE) first rejects it and then recommends it. But it can only be used in an arbitrarily defined epidemic. If you happen to have flu at other times then that's just too bad. Now Diggory et al have found that some people can't use the inhaler device properly.[1]

The next step will probably be to deny use of zanamivir to those who haven't been vaccinated against flu. In fact, it would almost certainly have been cheaper not to use mass vaccination for the majority who won't get flu than to prescribe zanamivir to those who do. But what would the other drug firms say to that—or, indeed, the Department of Health, whose officials refuse access to safety information on this year's batch of vaccines? Political correctness is an evidence free zone.

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Diagnosis of acute appendicitis

Appendicitis is a separate clinical entity in men and women

Editor—We read with interest the randomised controlled trial of ultrasonography in the diagnosis of acute appendicitis reported by Douglas et al.[1] This trial would add more to the literature if it were to acknowledge sex differences in the management of abdominal pain.

On every surgical take, the investigation of pain in the right iliac fossa differs between men and women. Often women have an ultrasound examination of the pelvis and abdomen primarily to exclude gynaecological or pelvic pathology. Conversely, men are much more commonly assessed by repeated clinical examination. Given the marked difference in the differential diagnosis of pain in the right iliac fossa in men and women, we argue that it should be seen as two separate clinical problems. To illustrate the above difference, we performed a retrospective analysis of 59 consecutive cases of pain in the right iliac fossa from the first three months of 2000 at the Royal Infirmary of Edinburgh. Of 30 men, three (10%) underwent ultrasound examination compared with 14 of 29 women (48%). Of those women who underwent ultrasound and subsequent appendicectomy, the ultrasound examination was usually negative (seven out of eight, one confirmed appendix mass) and had been used to exclude alternative diagnoses before appendicectomy.

A Medline search of the past two years did not find any papers in which men and women had been considered separately with regard to ultrasonography in appendicitis. Meaningful data can come only from trials that separate men and women. We would be interested to see if Douglas et al had separate data available.

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Author's reply

Editor—Thank you for raising the question of sex, which we did not address in the original article in the interests of being concise. It is well recognised that the diagnosis of appendicitis in women is harder, principally because of several gynaecological causes for pain.

In our study, 10 of 73 women (13.6%) in the control group had a non-therapeutic operation, compared with 9/73 (12.3%) in the intervention group. In men the numbers were 5/69 (7.2%) in the control group and 5/87(5.7%) in the intervention group. Numbers of cases of delayed treatment in association with perforation were as follows: in women, control 1/73, intervention 2/73; and in men, control 1/69, intervention 3/87.

Mean duration of stay was slightly longer in men, but did not differ between groups on analysis of subgroup by sex. Time to therapeutic operation differed between groups, much as it did in the overall analysis, but the difference did not reach significance in the analysis of the male subgroup.

Although there are sex differences that affect diagnosis and subsequent management, there is no evidence that ultrasonography improves outcomes in either subgroup.

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Cardiovascular events in users of sildenafil

Paper does not provide any reassurance

Editor—Shakir et al investigated the possibility of myocardial infarction being an adverse drug reaction among users of sildenafil.[1] However, their paper suffers from the problem that users of the drug are not representative of the general male population.

The authors point out that the proportion of men with diabetes among the users of sildenafil was four to five times higher than the national average. The overall mortality from acute myocardial infarction is four times higher among diabetic than non-diabetic men.[2] Thus standardisation by the general male population of England is not appropriate and will give an underestimate of the expected number of deaths in this cohort. The standardised mor-

tality ratio should be even less than the 69.9% quoted. Are we to believe that sildenafil protects against death from myocardial infarction?

More likely explanations of this result are, firstly, that the data gathered by prescription event monitoring suggest considerable under-reporting of events and are therefore not reliable and, secondly, that the number of patients in this cohort is too small. Normally, prescription event monitoring studies are considered complete when event data are available for 10 000 users of the drug (not 5600, as in this study). Thus no meaningful interpretation can be made of these data as regards the safety of sildenafil.

Finally, the paper includes a reference to a man who had a myocardial infarction after he took sildenafil and nitrate treatment for heart disease.[3] The data presented do not provide any reassurance for men who might use this combination of drugs, which could lead to severe hypotension.

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2 Lundberg V, Stegmayr B, Asplund K, Eliasson M, Huhtasaari F. Diabetes as a risk factor for myocardial infarction: population and gender perspectives. *J Intern Med* 1997;241:485-92.
3 Arora RR, Timoney M, Melilli L. Acute myocardial infarction after use of sildenafil. *N Engl J Med* 1999;341:700.

Authors' reply

EDITOR—Dunn queries our choice of comparator cohort. We consider the general male population to be appropriate for two reasons. Firstly, a valid external comparator cohort of sufficient size, comprising similar proportions of diabetic to non-diabetic men and for which cardiovascular mortality was reported, was not available; secondly, such comparisons are useful from a public health perspective.

We did not suggest that sildenafil is protective from myocardial infarction. On the basis of a standardised mortality ratio of 69.9% we believe that our conclusion was appropriate. The summary of product characteristics reminds practitioners that the drug should be used with caution in men with concomitant cardiovascular disease and avoided in those taking nitrates.[1] One possibility is that it is being prescribed appropriately.

Although the cohort of 5601 patients in the first phase of the prescription event monitoring study of sildenafil is smaller than the usual cohorts in such studies, it is not small compared with the number included in the premarketing development programme.[1] We emphasised that this was the first phase of a prescription event monitoring study aimed at identifying acute and relatively common events for consideration by interested parties. Our paper clearly stated that under-reporting was a potential weakness of the study.

Regarding the case report of myocardial infarction, when concomitant nitrate and sildenafil treatment were taken, Arora et al clearly referenced the regulatory authority's concerns at that time relating to use of sildenafil by patients with cardiovascular risk factors.[2] Dunn's comment regarding the concomitant use of nitrates is unjustified: we did not say or imply that this combination was safe.

Finally, we acknowledged that prescription event monitoring is a method of generating hypotheses and that further studies are needed to provide more definitive scientific explanations of these findings.

We believe that we have addressed the issues that Dunn raises. Our study provided no evidence of a higher incidence of fatal myocardial infarction or ischaemic heart disease in users of sildenafil. The second phase of this study will provide data on roughly a further 20 000 users of the drug followed up for a minimum of one year; this will result in greater statistical precision for our summary estimate.

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2 Arora RR, Timoney M, Melilli L. Acute myocardial infarction after the use of sildenafil. *N Engl J Med* 1999;341:700.

Hepatitis B, lamivudine, and HIV

EDITOR—Ryder and Beckingham reviewed the management and treatment of chronic viral hepatitis.[1] Lamivudine has a good safety profile and has been shown to be beneficial for patients requiring treatment for hepatitis B infection. It is, however, also a common agent used in the management of HIV infection. HIV and hepatitis B share similar risk factors for acquisition: intravenous drug use and sexual and vertical transmission. Therefore an appreciable proportion of patients are likely to be coinfected.[2]

To maximise efficacy and reduce the risk of the development of resistant virus, current guidelines recommend the use of at least three antiretroviral agents in the management of HIV infection.[3] If used in isolation, lamivudine leads to a rapid multiplication of resistant virus because of a mutation at position 184 in the reverse transcriptase gene, and potentially decreases future combination treatment available for that patient.[4] It is therefore extremely important in the management of hepatitis B infection to consider and offer an HIV test before starting treatment with lamivudine.

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Addison's disease should be diagnosed biochemically

EDITOR—The reports on Addison's disease in the *BMJ* emphasised the problems of diagnosing the condition at an early stage.[1 2] Addison's disease needs to be diagnosed as early as possible. Current protocols make the biochemical confirmation of the diagnosis comparatively straightforward for most patients. Considering this diagnosis in patients whose symptoms are vague and non-specific can be life saving.

Although we understand and sympathise with the statement that "Getting diagnosed is the hardest part of the disease,"[2] many patients can be diagnosed as having Addison's disease and be given corticosteroid "replacement" without a proper biochemical diagnosis. This is increasingly seen in the treatment of patients diagnosed as having the chronic fatigue syndrome, the postviral fatigue syndrome, or myalgic encephalomyelitis. Some of these patients have been shown to have mildly impaired pituitary-adrenal function but not in all studies[3]; it is generally believed that this is a consequence rather than a cause of the disorder.

Corticosteroid "replacement" has been used empirically in these situations, but it has not generally been found to produce dramatic changes. Certainly any use of this treatment should be closely monitored. The therapeutic benefits should be carefully considered in the light of the possible long term, deleterious consequences of inappropriate corticosteroid treatment, including the additive effects of pharmacological corticosteroids to endogenous production; this could cause not only long term suppression of the pituitary-adrenal axis but also adverse effects, such as hypertension and osteoporosis.

Without a formal diagnosis a young patient could face a lifetime of inappropriate corticosteroid use. Although the diagnosis of Addison's disease should be seriously considered against a background of malaise and fatigue, confirmation should be rooted on firm biochemical footing.

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Fetal growth markers may show nutritionally mediated effect

EDITOR—Robinson's editorial on the first world congress on the fetal origins of adult disease reflects just one element of the extensive programme of research investigating this hypothesis.[1] The quantity and quality of epidemiological data suggest irrefutably that there is some association between prenatal factors and later cardiovascular disease, diabetes, and other chronic conditions. The assertion that less than optimal maternal nutrition underlies these observations is, however, far from secure. Studies of well nourished populations in the United Kingdom and rural populations with poor food intake across the globe indicate that the influence of nutritional status on birth weight is small.

Robinson largely overlooked the element of fetal origins research that relates to animal studies. Experiments with rats, guinea pigs, and mice indicate that maternal nutrition can be an important determinant of adult cardiovascular disease and glucose metabolism.[2] The feeding of low protein diets in rat pregnancy, for example, promotes glucose intolerance, insulin resistance,[3] high blood pressure, reduced aortic compliance, remodelling of arterial structure, reduced renal reserve, dysfunction of the hypothalamic-pituitary-adrenal axis, altered renin-angiotensin status, and impaired immune functions.

All of these effects may be observed without any major evidence of fetal growth retardation or disproportion at birth.[2] This suggests that markers of fetal growth determined at birth in the epidemiological studies of Barker and others are actually crude indicators of a more subtle nutritionally mediated effect.

After a decade of major progress and investment of funds the coming together of research groups at this world congress in India has provided an opportunity to take stock and plan for the future. A major priority for further investigations must surely be to avoid repetition and duplication of the epidemiological and experimental studies which are already complete. The possible associations between specific nutrients or dietary patterns in pregnancy and later disease need to be established. This will finally allow the development of a new age for health promotion.

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Adult obesity depends on genes and environment

EDITOR—The editorial by Sørensen and Echwald recognises the substantial effect of environmental factors on obesity but, surprisingly, gives the impression that childhood environment is not important.[1] It cites twin and adoption studies that confirmed the absence of effects of the environment in which they were raised.[2 3]

The studies cited, although showing minor effects, did not claim to be able to rule out the influence of childhood environment. One emphasised that the results were based on "persons living under a particular range of environmental conditions" and might be different under other conditions.[2]

The other acknowledged that the heritability estimates did not exclude environmental pathways and that expression of heritability may depend on the environment.[3] The difference in childhood environment between twins and siblings reared apart through adoption is likely to be small compared with that among the generality of children of similar age.

Population based studies (with social position being used as the measure of early environment) show a clear effect of childhood environment on the risk of obesity in adulthood. This was seen in the Medical Research Council's national survey of health and development[4] and the Whitehall II study.[5]

The Medical Research Council's survey (1946 birth cohort) found that body mass index at age 36 was significantly associated with parents being in manual or non-manual occupations. The percentage overweight or obese for men was 46% (manual) and 33% (non-manual); for women it was 36% (manual) and 21% (non-manual). Differences persisted after account was taken of social class in adulthood.[4]

The Whitehall II study also showed that childhood social disadvantage was associated with an increase in body mass index in adulthood. Participants with fathers in social class 5 had significantly greater body mass index than those in social class 1: men 0.55 kg/m^2; women 1.42 kg/m^2.[5] The consequences of childhood social class varied according to subsequent social trajectory.

The effect of childhood environment on probability of adult obesity is thus not a fixed effect but depends on the combination of genes, childhood environment, and later life experience.

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Liver cirrhosis is risk factor for pyogenic liver abscesses

EDITOR—In their article on liver abscesses Krige and Beckingham emphasised the role of impaired immunity in the pathogenesis of pyogenic liver abscess.[1] They also reported that the prognosis for patients with liver abscesses depends on concomitant or previous severe illnesses.

They did not, however, mention the association between liver abscesses and liver cirrhosis. Liver cirrhosis is often associated with severe immunodeficiency, and in one case series up to 13% of patients with pyogenic liver abscesses had had cirrhosis.[2]

In a recent study based on the entire Danish population (roughly 5.2 million) we reported the risk and short term prognosis of pyogenic liver abscesses.[3] The Danish national registry of patients contains information on virtually all hospital discharge diagnoses in Denmark since 1977. In a nationwide cohort of 665 patients with liver abscess 3.2% had had liver cirrhosis as an illness.

The risk of liver abscesses in patients with alcoholic cirrhosis and non-alcoholic cirrhosis compared with the general population was increased 15.5-fold (95% confidence interval 8.2 to 26.5) and 15.7-fold (6.8 to 30.9), respectively. In addition, liver cirrhosis was a risk factor for death, since the 30 day fatality rate increased 4.3-fold (1.2 to 15.2) and 4.8-fold (1.0 to 22.4) in patients with alcoholic cirrhosis and non-alcoholic cirrhosis, respectively, compared with the general population.

Liver cirrhosis is therefore a strong risk factor for pyogenic liver abscesses and a risk factor for death. Loss of hepatic filter function, impaired immunity, and frequent abdominal infection and septicaemia in patients with cirrhosis are probably factors responsible.

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Responsibilities of sponsors are limited in premature discontinuation of trials

EDITOR—The contributions by Lièvre et al and Pocock and Evans make important points about the ethical problems surrounding early termination of trials for non-scientific reasons.[1 2] But their argument about the responsibilities of sponsors goes too far.

The Declaration of Helsinki makes it clear that sponsors and investigators do have obligations to the participants enrolled into the trial. These include fair treatment, avoiding exploitation and unnecessary harm, and treating patients with respect. Among other things, this entails not starting a patient off on a treatment, observing that the treatment is beneficial, and stopping the treatment of that patient for purely commercial reasons. Sponsors and investigators should recognise that the risk assumed by trial participants, and the altruism of such participants, places obligations on sponsors to complete a beneficial course of treatment even after the close of the trial. The argument is more complex when considering treatment for chronic disease or for prevention of disease in the long term.

None of this implies an obligation on sponsors with regard to patients not yet randomised or the patient population at large. There is no obligation on sponsors to conduct trials or market their products where there is no foreseeable profitable market for them. Moreover, sponsors normally have to choose among various products to develop and then market, and this choice is always in the light of opportunity costs.[3]

There is a public interest in completing trials, in having the best evidence base available and ensuring that treatments are available for as wide a range as possible of conditions. This public interest does not, however, impose moral obligations on companies. Companies are a social solution to meeting this collective interest, harnessing the power of competition to deliver treatments efficiently. The problem Lièvre et al identify is a problem of market failure, rather than of morals.

The solution is a political one: states have a responsibility to address market failure. This lesson has been learnt in the case of orphan drugs; we should generalise it to apply to other cases of market failure in research and development.[4]

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Fertility treatment in HIV needs multidisciplinary team

EDITOR—There is a wide difference between rejecting all requests for artificial reproductive treatment in couples infected with HIV or accepting them all, as suggested by Gilling-Smith et al in their editorial.[1] Although sperm washing may reduce the risk of contamination, the total number of cases published and documented is much lower than the number reported in the editorial and is insufficient per se to ensure that the risk of contamination has disappeared. Moreover, only sperm tested for the absence of HIV RNA and DNA can be used. In these cases, the option of intracytoplasmic sperm injection rather than intrauterine insemination should also be discussed since in this procedure only a restricted number of spermatozoa will be used. Until now, sperm donation remains the first choice of fertility treatment for men who are HIV positive. In HIV positive women, the risk of vertical transmission may be reduced to less than 2% when all favourable health indicators are present, but for other women and for those who will develop obstetric complications (such as premature rupture of membranes) these risks may be much higher and should also be discussed. Finally, there is a possibility of misinterpretation when one compares the magnitude of the risks of vertical transmission to those of congenital malformations since these separate risks should be combined.

At our institution a multidisciplinary team including an obstetrician, an AIDS specialist, a paediatrician, a fertility specialist, and a psychiatrist therefore evaluates the motivation of child desire and informs the couple about all the risks (risks of transmission when using washed spermatozoa, risks of multiple pregnancies in artificial reproductive treatment, the need for antiviral prophylaxis and its teratogenic effects, contraindications of amniocentesis, and breast feeding, utility of caesarean section, and prognosis of an infected child). The perception and acceptance of these risks by the couple are evaluated.

The argument that denying such a couple artificial reproductive treatment will result in an increased transmission rate owing to unprotected intercourse is fallacious. The couple should not be denied fertility and transmission counselling and should be socially guided in their fertility problems. Long term studies about the impact on HIV transmission in serodiscordant couples seeking reproduction are needed. Although remarkable progress has been achieved in HIV prognoses, it is crucial to provide thorough information and evaluation by a multidisciplinary team in order to individualise the choice or absence of assisted reproductive technologies and provide follow up.

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Iraqi doctors appeal for help from doctors in other countries

EDITOR—The Iraqi Medical Association would like to thank the BMA for the donation of medical books and journals that it made to Iraqi medical schools and the association last year. Because of the sanctions on Iraq, however, none of the books have arrived yet and we have received only a few copies of the *BMJ*.

The sanctions have led to the deterioration of what was an extremely good national health service. In 2001, thousands of Iraqis are still dying from malnutrition, infectious diseases, and the effects of shortages or unavailability of essential drugs. More and more children are dying from cancer, probably related to contamination of the environment with depleted uranium.

Iraqi doctors are suffering greatly from the intellectual embargo. Recent medical textbooks and journals are difficult to obtain. It is extremely difficult for Iraqi doctors to travel abroad to attend medical conferences or training courses. In hospitals and clinics our doctors are facing great difficulties providing good medical service to their patients.

We appeal to the BMA and other doctors to help their Iraqi colleagues by:

- Publishing facts about the medical and social situation in Iraq
- Inviting Iraqi doctors to attend international and national meetings and training courses outside Iraq
- Inviting interested British doctors to visit Iraq and participate as lecturers in the intensive, up to date medical courses that the Iraqi Medical Association is planning to arrange
- Donating recent medical electronic publications to the Iraqi Medical Association (Cath02@uruklink.net).

The Iraqi Medical Association appeals to all readers to help get sanctions lifted completely from Iraq as this is the only real solution for the suffering of the Iraqi people.

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