hepatitis A is not cost effective for society or the person concerned.¹ No such study should group all countries outside Europe, North America, and Australasia into the same category of risk regardless of the itinerary and duration of visit and the lifestyle followed. The authors' observation that 68% of travellers to these areas are not immunised against typhoid is suspect as only the number of vaccine phials for which general practitioners were reimbursed was used to estimate the number of immunised travellers. Many other travellers are already protected, having been immunised within the previous three years (30% at my travel clinic). In addition, the intradermal route allows up to 15 booster doses to be obtained from one phial; many practitioners purchase phials themselves, avoiding unnecessary visits for prescriptions, and increasingly vaccines are administered by NHS hospitals and private clinics. Other travellers are intentionally not immunised because the risk is minimal—for example, in Japan, Singapore, and the West Indies or during brief stays elsewhere in good accommodation. Perhaps only 20%—not 68%—of those at risk may not be immunised.

For hepatitis A the authors considered only prescribed commercial immunoglobulin, not that supplied by the blood transfusion service (10 000 doses annually in the west of Scotland alone). Most trips abroad are brief, for which only 250 mg, half the standard 5 ml dose, is necessary. Also, two doses (more recently one of active vaccine)—not three as used in the calculations of cost—are necessary for fully primary immunisation.

In the calculations of total illness, those episodes occurring abroad are not considered. Confining the total number of cases to notifications confirmed by a laboratory, will yield a poor estimate, especially for hepatitis A: many practitioners avoid non-essential venepuncture, particularly in children. The estimate of 50% underreporting for typhoid and hepatitis A is probably far too small.

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1 Behrens RH, Roberts JA. Is travel prophylaxis worthwhile? Economic appraisal of prophylactic measures against malaria, hepatitis A, and typhoid in travellers. *BMJ* 1994;309:918-22. (8 October.)

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Assumptions were confusing

EDITOR,—We have performed economic evaluations of prophylaxis against hepatitis A in travellers, and two of R H Behrens and J A Roberts's main conclusions¹ are in line with our findings^{2,3}—namely, that hepatitis A vaccination is not cost saving for the average traveller and that vaccination becomes more cost effective than immunisation with human immunoglobulin when the expected frequency of travel exceeds two occasions in the next 10 years. Despite this agreement, we have some difficulties with several assumptions and statements made in the article.

Firstly, the authors state that the cost-benefit ratio of (passive and active) immunisation increases as the seroprevalence reduces to 9.7% (instead of 30%). This seems nonsensical: it can never be the case that the attractiveness of a preventive action decreases when the proportion of susceptible subjects increases since costs remain the same but benefits increase as more infections can be prevented. Secondly, there is substantial confusion regarding the required threshold incidence (or risk) of hepatitis A that would give a cost-benefit ratio of one. The authors state that this

would occur with 1550 cases annually. This is about six times their reported number of cases of 288 but only three times the "corrected" number of 576 in table I. Nevertheless, the authors say that even if the assumed incidence of 0.05% increased sixfold to the incidence of 0.3% per visit reported for Swiss travellers "the costs would still exceed the benefits by a significant amount." How can these two contradictory statements be reconciled? Thirdly, the authors have performed a cost-benefit analysis but use the terminology carelessly when they say that hepatitis A vaccination is not cost effective (in the abstract) or even is inefficient (in the discussion) when they mean not cost saving.

Finally, we think that it is important to specify further the indications for prophylaxis against hepatitis A and agree that it is necessary to design "a suitable protocol which would target high risk non-immune groups." We have derived some recommendations regarding optimal choices in various circumstances based on a cost-effectiveness analysis elsewhere.⁴

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- 1 Behrens RH, Roberts JA. Is travel prophylaxis worthwhile? Economic appraisal of prophylactic measures against malaria, hepatitis A, and typhoid in travellers. *BMJ* 1994;309:918-22. (8 October.)
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Journals should develop guidelines for economic evaluations

EDITOR,—The cost-benefit analysis of travel prophylaxis reported by R H Behrens and J A Roberts is flawed.¹ Among other things, such an analysis requires a monetary value to be placed on all the benefits resulting from a health care intervention.² The cost-benefit ratios presented by the authors, however, exclude any estimate of the main components of the benefits of the vaccination programmes under consideration—namely, people's willingness to pay to avoid the morbidity associated with the diseases. This means that the cost-benefit ratios reported and all discussion and conclusions based on them are unsafe and could seriously mislead decision makers.

The paper raised the important issue of how the interests of decision makers in health care and of patients can be safeguarded through measures to ensure that economic evaluations are conducted to high methodological standards. Recently, the pharmaceutical industry worked in partnership with the government to produce guidance on good practice in economic evaluations of medicines either sponsored or undertaken by pharmaceutical companies.³ Similar standards should be applied to all researchers. The editors of peer review journals such as the *BMJ* have a potentially important role in upholding such standards. There would be enormous benefit to be gained from journals developing clear policies on the acceptance of economic evaluations, including guidelines for authors.

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- 1 Behrens RH, Roberts JA. Is travel prophylaxis worth while? Economic appraisal of prophylactic measures against malaria, hepatitis A, and typhoid in travellers. *BMJ* 1994;309:918-22. (8 October.)
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**The *BMJ* is currently working with an international group of health economists to develop guidelines for economic evaluations. These should be useful to authors, editors, reviewers, and readers.—ED, *BMJ*

Reporting of air pollution levels

EDITOR,—Two articles in the issue of 22 October reported levels of air pollutants and their possible health effects.^{1,2} Gregor Campbell-Hewson and colleagues refer to ozone levels being "at a two week high" and report a figure of "45 ppb, compared with a daily average of 28.7 ppb over the preceding and following weeks."¹ Was this value an hourly maximum value for that day, the eight hour mean (for which the Expert Panel on Air Quality Standards has recently set a new standard of 50 ppb³), or a 24 hour mean? On how many days over the preceding and following weeks (I presume one week each side) was an equivalent value recorded? The given value is uninterpretable as it stands.

In the other article Alexander Dorozynski falls into an identical trap, reporting that health problems were seen in Paris "as soon as levels of pollution... rise 100 $\mu\text{g}/\text{m}^3$ above the maximum levels said to be acceptable for Europe."² Again it is unclear whether he is referring to hourly or daily measures. He also does not state the form of particle measurement that was used. In Britain particulate matter of <10 μm mass median diameter exceeds 100 $\mu\text{g}/\text{m}^3$ as a daily mean value only during episodes of air pollution. If Dorozynski is using the daily mean guideline in winter (111 $\mu\text{g}/\text{m}^3$) then an increase of 100 $\mu\text{g}/\text{m}^3$ over that value will only very exceptionally be achieved.

With so much inaccurate, and at times scare-mongering, reporting of possible health effects of pollution in the lay press the medical press must ensure that levels of air pollution are reported adequately and accurately. Whenever a measurement of air pollution is recorded the sampling time must be given, and when reference is made to guideline levels these levels should be specified so that the measured value can be compared with them.

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- 1 Campbell-Hewson G, Cope A, Egleston CV, Sheriff HM, Robinson SM, Allitt U. Epidemic of asthma possibly associated with electrical storms. *BMJ* 1994;309:1086-7. (22 October.)
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Pigments in breast fluid

What are they?

EDITOR,—The article on assessing symptoms of breast diseases contains a photograph showing that physiological breast secretions, like fluid from breast cysts, range in colour from white to yellow to green to blue-black.¹ The pigmentation is thought to have no diagnostic importance.² But what causes it? About the only truly green compound produced in humans is the bile pigment

biliverdin, which imparts a green colour to breast milk in some animals.³

I have examined a sample of dark green fluid from a human cyst by absorbance spectroscopy and high pressure liquid chromatography; this showed that the green pigment of the fluid, which has a broad, featureless optical absorption band with a maximum near 590 nm, is not biliverdin. Nor does it seem to be a heme pigment or a porphyrin. A cursory computer search of the literature failed to provide any clues. I wonder whether any readers can shed some light on the origin, structures, importance, or function of these mammary chromophores.

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- 1 Dixon JM, Mansel RE. ABC of breast diseases: symptoms assessment and guidelines for referral. *BMJ* 1994;309:722-6. (17 September.)
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Authors' reply

EDITOR,—The breast is thought to be a modified apocrine gland. Secretions from the apocrine glands show the same range of colours as that of physiological breast secretions and fluids from breast cysts.¹ Breast secretions of a darker colour (deep yellow, brown, green, and blue-black) contain significantly higher concentrations of cholesterol, cholesterol 5,6-epoxides, oestrogens, and fluorescent products of lipid peroxidation.^{2,3} Patients who smoke are also more likely to have darkly coloured breast secretions. In white women a progressive increase in the proportion of dark coloured breast secretions has been noted with increasing age; this trend was not found in black women.³ The proportion of women with dark coloured breast secretions seems to be lower in women of Chinese and Japanese origin than in white or black women.³ The colouration of breast secretions is thought to represent pigmented products of apocrine gland secretion, lipofuscin complexes of peroxidized lipoprotein, breakdown products of haemoglobin, and, possibly, secretory products related to diet.

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- 1 Hurley HJ, Shelly WB. *The human apocrine sweat gland in health and disease*. Springfield, IL: C C Thomas, 1960.
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Diabetes in the developing world

EDITOR,—As a physician with origins in east Africa and with continuing medical links in that region, I was heartened by K G M M Alberti's concern for those who have a "right to life and at a small cost per patient by Western standards."¹ The difficulty in dealing with what is essentially a long term management challenge (a diabetic patient presenting at age 17 may well require insulin for

another 40 years or so) rests in being able to guarantee the patient a relatively uninterrupted supply of a drug for a lifetime; this is a far cry from treating a single episode of an attack of malaria or an acute diarrhoeal event in a child. As Alberti points out, to count on the generosity of donors or the largesse of pharmaceutical companies for indefinite periods is both undesirable and possibly unrealistic. To hope that most African governments can divert up to \$150 annually per patient to sustain each individual is clearly, however, even more improbable. With costly pharmaceuticals—where benefits accrue to the minority at the expense of, say, low cost, high impact programmes in primary health care for the majority—even the most well meaning of governments among the so called least developed countries would be hard pressed to justify such a diversion of scarce financial and health care resources. The issue in diabetes is further complicated by the lifetime need for medical support and education, foot care, eye care, and dietary needs, which the average rural African may well find a challenge to pursue on his or her meagre income.

Alberti's editorial raises interesting issues relating to the ethics of initiating, say, insulin treatment procured through an international charity with no guarantee that support can be sustained as the patient grows older and presumably assumes greater personal and economic commitments. Should interested charities that agree to provide this support "profile" the ideal patient to support (as we do with candidates for cardiac and renal transplants) on the premise that long term commitment to a few is superior to uncertain commitment to all? My sense is that, within the spectrum from what can be done to what must be done, the provision of daily insulin to rural Africans through local government effort must rate rather low in the least developed countries. Most of those people who are afflicted will have to continue to look to international organisations, which in turn must also get their priorities right.

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- 1 Alberti KGMM. Insulin dependent diabetes mellitus: a lethal disease in the developing world. *BMJ* 1994;309:754-5. (24 September.)

Pharmaceutical donations to eastern Europe

EDITOR,—We are concerned that some hospitals and general practitioners in eastern Europe may be receiving unhelpful and potentially hazardous donations of drugs from western European aid organisations. We are particularly interested in the situation in Romania, where we have worked.

The public health service in Romania is chronically short of drugs. Although modern drugs are now available in Romania, many of them are too expensive for most people, who still have very low incomes. Thus, understandably, many western European charities have been asked for and have provided donations of medicines. Unfortunately, in many cases donations of drugs are unsolicited and medical advice is not sought. The drugs sent seem to be surplus to the requirements of their donors, and all too often they are inappropriate for the needs of the recipients (for example, adult doses may be sent to a paediatric unit). Not uncommonly, the medicines are time expired or partly used. The experiences of various bodies in eastern Europe, including the World Health Organisation, indicate that 45% or more of donations of drugs are likely to be unusable, irrational, or hazardous in some way.¹

We have come across cases in which drugs were

used in ways that, in Britain, would be regarded as potentially hazardous. Assays of therapeutic concentrations are not generally available in Romania, and basic biochemical tests (of renal and hepatic function) are often unreliable. The donation of drugs with a narrow therapeutic range (for example, aminoglycosides) needs careful consideration. Up to date information on drugs is scarce in some parts of Romania, and drugs from Britain or other parts of Europe may have potencies that differ from those of their local equivalents. There is also a risk that information may be mistranslated, with possibly disastrous consequences. Carcinogenic cytotoxic drugs may be requested without the safeguards for handling and use that apply in Britain. Gloves, aprons, and goggles may be lacking, and staff are often unaware of the need for special care, exposing themselves and their patients to unnecessary risk.

Drugs for patients with chronic conditions are in particular demand, but charities need to look to the future and weigh up the value of starting a treatment that they may not be able to continue. Romania will not be self sufficient in pharmaceuticals for some time.

Donations of medicines to eastern Europe may be valuable and appropriate, but only if careful consideration is given to the choice and destination of drugs. Professional advice should be sought, in both the donor and the recipient countries, from people experienced in assessing this type of need. The present uncoordinated system is doomed to continue the inappropriate and hazardous giving outlined above.

In general it is proper for charities to exercise autonomous control over their giving; we believe, however, that pharmaceuticals require special treatment. A system should exist for coordinating donations of pharmaceuticals within Britain. We thus propose the formation of a British Medicines Advice Group to work with charities that wish to donate drugs to Romania and other countries of the former eastern bloc. Such a group could help charities to manage donations of medicines more appropriately and would probably achieve improved safety, better targeting, reduced waste, and greater equity.

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- 1 World Health Organisation. *Think before you send*. Zagreb: WHO Regional Office for Europe, 1994. (Press release.)

Advice to authors

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