LETTERS

Rationing in developing countries

SIR,—Rationing in health care is increasingly being discussed in developed countries.[1,2] In state health services in developing countries it has existed for decades under a different name—namely, shortages. Attempts at rationing, especially in developing countries, however, are like the person pulling drowning children out from the stream without being able to do anything about the person upstream throwing them in. The cost of drugs is a large component of the health care budget in developing countries, accounting for up to 40% of the total[3]; the annual trading deficit in pharmaceuticals of these countries was estimated to be $4 billion 10 years ago.[4] In developed countries drugs account for about 10% of the health care budget.[4]

To select just one example from pharmaceuticals, the net price of a Zantac tablet (150 mg) manufactured and sold in the United Kingdom is about 50p[5]; this same tablet is sold in Sri Lanka for 30p and, as in the United Kingdom, is the only brand of ranitidine available. The difference in cost could be due to the manufacturers' desire to provide drugs at reasonable cost or the market conditions in Sri Lanka not permitting a higher price, or both. In India the same manufacturer produces ranitidine with a slightly different brand name, Zinetac, presumably with the same standard of good manufacturing practice that it maintains worldwide. The net price of this ranitidine (Zinetac), however, is about 5p; other brands of ranitidine are available in India. Because of company policy the cheaper ranitidine is not imported into Sri Lanka; the company does, however, import other products from its Asian subsidiaries. The patent laws do not allow third parties to import the Indian ranitidine into Sri Lanka. To put the costs in perspective, a labourer earns the equivalent of about £1 a day in this part of the subcontinent.

This type of control resulting in much higher prices for pharmaceuticals is the rule rather than the exception. Multinational pharmaceutical companies with headquarters outside Asia register and export the more expensive products to Sri Lanka (database of pharmaceuticals registered in Sri Lanka, department of pharmacology, Faculty of Medicine, Colombo, Sri Lanka). The subsidiaries of these companies in India produce and sell the same product at a fraction of the price for use in that country only. As with ranitidine, the patent laws of the developed countries (accepted also by Sri Lanka) prevent the cheaper product being imported.

Richard Smith made a convincing plea for the discussion on rationing of health care in developed countries to be brought out into the sunlight.[6] In developing countries such matters are still in darkness, an ideal environment in which may thrive the avaricious streak of an industry claiming to help to alleviate disease.

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**We sent this letter to Glaxo, whose reply is given below.

SIR,—Glaxo agrees that there is reason for concern about the financing of health care in the developing world. Throughout the developing world many people do not have sufficient access to health care. The pharmaceutical industry should not, however, be portrayed as a villain in this. Glaxo and other companies have a considerable commitment to improving health care in the developing world.

It is not appropriate to consider pharmaceutical companies' contribution to health care—and to label the industry avaricious—on the basis that they price their medicines similarly in developing and developed countries. Glaxo establishes prices with the goal of providing good value to patients, health care providers, and society while also generating revenue to fund future innovation. On this basis Glaxo believes that its prices are fair and that having a separate pricing structure for developing countries is inappropriate. (India is mentioned as a low priced market. Most countries, including Sri Lanka, realise that adequate patent protection is essential to maintain a viable pharmaceutical industry. India apparently does not share that view. On 29 April the United States imposed sanctions on India for its refusal to provide patent protection for foreign pharmaceuticals.)

Krisantha Weerasuriya and Colvin Goonaratne state that pharmaceuticals are a large component of the health care budget in developing countries. But focusing on the proportion of the budget spent on pharmaceuticals misses the point that pharmaceuticals are often cost effective in relation to other alternatives.

Glaxo's efforts to improve and expand access to health care in the developing world take several forms. For example, Glaxo has funded a chair in molecular parasitology at Cambridge University. At the local level Glaxo's companies organise and support efforts to improve distribution systems for medicines and to advance general health education. Local initiatives in Sri Lanka include medical education programmes, a public education programme on asthma, and contributions to hospitals and to regional medical camps for the country's poor. By its presence Glaxo also contributes to economic growth. In Sri Lanka it has about 230 employees. It manufactures medicines in many countries, such as Bangladesh, where it employs 800 people. The economic impact of the industry may best be illustrated by Mexico, where the pharmaceutical industry employs over 45 000 people.[1]

The pharmaceutical companies, by working with officials in the developing countries and through continued commitment to economic development there, help to improve the quality of and access to health care.

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1 Mexican 1990 Pharma market. *Scrip* 1992;No 1684:20.

Measles, mumps, and rubella vaccination

SIR,—Recent authors have reported the continued occurrence of measles in older children in Fife and Somerset and argued that, to ensure elimination of disease, measles, mumps, and rubella vaccine should now be given to secondary school children in addition to 1-2 year olds.[1-3] The occurrence of measles in older, unvaccinated children in areas with previously poor uptake of single antigen measles vaccine is to be expected in the short term, and extending the original measles, mumps, and rubella catch up programme for younger children to older age groups may be indicated as an interim measure in such areas. Nationally there is no indication that cases in older subjects have a major role in maintaining transmission (table). The increase in the proportion of cases in older age groups since the introduction of measles vaccine in 1968 is the expected consequence of a mass immunisation programme targeted at young children.[4]

Although vaccinating secondary school children may provide some interim local benefit, advocating this as a national strategy for elimination is in our view misguided. Observations from other countries, supported by calculations based on mathematical models of viral transmission, suggest that measles can persist despite coverage of over 90% with a single dose and that additional vaccination will be required to achieve elimination. To be successful, however, this must reach those not already vaccinated and at an early age. Offering measles, mumps, and rubella vaccine to secondary school children will not achieve this. Firstly, uptake of rubella vaccine in 10-14 year old girls is lower than that of measles, mumps, and rubella vaccine in 2 year olds. Secondly, similar social factors will probably determine compliance at each dose, and the net benefit of the second dose will probably largely be seroconversion in the few children in whom the initial vaccination failed. Thirdly, to delay revaccination for 10 years would be beneficial only if immunity induced by vaccination waned, but this does not seem to be an appreciable problem.

Alternative strategies for keeping the susceptible pool below the minimum necessary to maintain

Measles notification rates 1967-91, England and Wales

	Rate/100 000			% Of total		
Age (years)	1967	1987	1991	1967	1987	1991
<1	2237·4	574·4	381·0	4·0	9·2	27·5
1-4	7763·4	666·3	153·2	56·7	41·0	43·3
5-9	4450·5	511·7	49·4	36·4	38·1	16·6
10-14	248·8	87·3	19·5	1·8	6·4	6·1
15-24	44·5	17·7	5·1	0·7	3·4	4·0
≥25	4·9	2·5	0·7	0·3	2·0	2·4

Breakdown by age available for January-June only.

transmission should therefore be explored. As cases in infants now seem to be making a considerable contribution to endemic transmission (table), one approach would be to offer infants early measles vaccination before giving measles, mumps, and rubella vaccine in the second year of life. Studies to determine the serological response to early vaccination in infants of vaccinated and naturally immune mothers and the accuracy of a clinical diagnosis of measles in infants and older age groups are under way, together with theoretical studies to explore the impact of such a strategy.

An epidemiologically and logistically different approach to routinely offering two doses would be to attempt to vaccinate all subjects in a wide age range within a short time and thereby interrupt transmission. This has recently been done in the English speaking Caribbean, where over 95% of all children aged 1-15 in eight of the 17 islands were vaccinated within one month.[5] To ensure elimination this initiative must be repeated periodically, the interval and targeted age groups being decided on the basis of epidemiological data such as the age specific prevalence of the antibody,[6] and results of theoretical studies.

Clearly, further work is required to provide a sound scientific basis for deciding future policy. We suggest that in the short term the cost effectiveness of offering measles, mumps, and rubella vaccine to secondary school children should be decided locally on the basis of a district's previous uptake of measles vaccine and present age specific notification rates.

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Storing vaccines at the correct temperature

SIR,—Yogini Thakker and Sheila Woods[1] and Philippa Lewis[2] discuss storage of vaccines and management of the cold chain; Lewis has developed temperature record charts and guidelines. It seems that the developed world could learn some lessons from the Third World about managing immunisation programmes.

I have recently been working on an immunisation programme for Afghanistan, where health workers and vaccinators of varying educational backgrounds and limited training carry out immunisation. Most health workers can quote the correct storage temperatures for vaccines and know how these temperatures should be maintained and monitored while the vaccines are being transported from manufacturers in Europe to remote villages in Afghanistan. These journeys may take many months and present immense logistical problems owing to wide variations in temperature; lack of transport, roads, and power sources; and war. Most vaccine, however, arrives and is stored in good condition as monitored by the vaccine monitor cards and freeze watches that accompany supplies of vaccine.

Lewis and all those working in immunisation would be advised to consult the excellent publication *Immunisation in Practice: a guide for Health Workers who Give Vaccines.*[3] The EPI (expanded programme of immunisation) division of the World Health Organisation also supplies training material on all aspects of immunisation, including the use of cumulative temperature indicators such as the vaccine monitor card and freeze watch. This is the only means by which cumulative exposure of vaccine to both high and low temperatures can be checked during transport and storage. The effectiveness of this system of monitoring the cold chain has been repeatedly shown in developing countries, and I find it difficult to comprehend why the same standards of care are not adhered to in Britain. Perhaps in Britain some outbreaks of diseases that are preventable by immunisation could be explained by the reduced potency of vaccines damaged by storage at incorrect temperatures.[4]

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Immunisation of children born to mothers positive for anti-HBe

SIR,—We cannot agree with S V Beath and colleagues about the consensus view on hepatitis B immunisation that they describe.[1] The British Paediatric Association,[2] the American Public Health Association,[3] the Department of Health,[4] and the *British National Formulary*[5] recommend a full course of vaccine and hepatitis B immunoglobulin for all children born to mothers who are positive for hepatitis B surface antigen irrespective of whether the mothers are positive for antibody to hepatitis B e antigen (anti-HBe). All these organisations emphasise the increased infectivity of people who are positive for hepatitis B e antigen but clearly state that detectable anti-HBe does not exclude infectivity; they state only that the risk is reduced.

Evidence of viral replication has been clearly shown in people positive for anti-HBe.[6] Even if a mother has recently developed anti-HBe lack of infectivity cannot be presumed. Although the risk of infection may be low, the potential hazards are great.[1] The consensus is clear: all children born to mothers positive for hepatitis B surface antigen should be given prophylaxis.

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Harm minimisation for drug misusers

SIR,—John Strang and Michael Farrell provide valuable advice on managing drug misuse in their editorial on harm minimisation.[1] We wish to comment, however, on their statement that use of the pure opioid antagonist naloxone is probably associated with only minimal risk.

Though respiratory depression in opiate overdose may be fatal, using naloxone to reverse this central hypoventilation is not without hazard. Several authors have documented serious side effects associated with naloxone. These include the precipitation of withdrawal symptoms,[2] intense pressor responses, tachycardia, and pulmonary oedema. In one report two patients died immediately after receiving naloxone, probably because of release of catecholamines.[3]

In addition, the duration of action of naloxone given intramuscularly or intravenously is only 30-40 minutes. The opiates commonly misused, however, have a much longer duration of action, and their effects may re-emerge when the effect of the naloxone has worn off. Indeed, the knowledge that naloxone antagonises opiate overdose might encourage excessive self administration of opiates.

Though we agree that distributing ampoules of naloxone could be of some benefit in harm minimisation, we believe that the potential hazards outweigh this benefit.

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2 Popper C, Kellen GD, Cunningham G. Naloxone hazard in drug abusers. *Lancet* 1989;ii:446.
3 Andree RA. Sudden death following naloxone administration. *Anesth Analg* 1980;**59**:782-4.

SIR,—We disagree with Michael Farrell and John Strang's rather proprietorial and parochial views about methadone treatment for opiate addicts.[1] They note that while "the Netherlands has relied on a harm reduction model with methadone maintenance, . . . the British programme has relied on shorter term use of methadone" and make a similar implication in their editorial on harm minimisation for drug users.[2]

It is true that many British clinics and general practitioners are now reluctant to prescribe long term maintenance despite the impressive evidence that generous dosage and flexibility about the duration of treatment are prerequisites for success.[3-6] This reluctance, however, developed fairly recently and reflects morality and short term economics rather than therapeutic considerations. There are still NHS clinics that do not force patients off methadone before they are ready or offer generally inadequate and unpharmacological doses.

In any case, the authors' own unit has maintained a group of addicts on high doses of injectable heroin since the mid-1960s.[7] We know of other NHS clinics that officially offer only short term methadone but are prepared to maintain a few patients indefinitely. The United States, which in some respects is very restrictive about methadone, nevertheless has several hundred clinics, both public and private, that prescribe methadone long term.

One of us directs a private addiction service that includes an oral methadone programme (average dose 79 mg a day). Far fewer patients would have to seek private treatment if they were not forced to endure inadequate doses or compulsory reductions