fore repeated at a serum dilution of 1:20 after absorbing with double the quantity of anti-G antibodies, and unequivocal positive results for parvovirus B19 IgM were then obtained. It would be unfortunate if high concentrations of parvovirus B19 IgG were to mask the laboratory confirmation of acute infection with less sensitive techniques when the diagnosis was suspected clinically.

With regard to the management of an outbreak of parvovirus B19 infection, we have prepared a fact sheet for professionals and an explanatory leaflet for parents which we are happy to make available.

D IGOE
B GILMER
H JOHNSON

Eastern Health Board, Community Care,
Vergemount Hall,
Dublin 6,
Republic of Ireland

Regional Virus Laboratory,
Royal Victoria Hospital,
Belfast BT12 6BN

1 Pattison JR. Human parvovirus B19. *BMJ* 1994;308:149-50. (15 January.)

Consider short courses of antibiotics

EDITOR,—The Department of Health's determination to reduce prescribing costs will leave many general practitioners looking for ways to do this without harming their patients; perhaps they should consider the duration of the courses of antibiotics that they prescribe for uncomplicated infections. The preferred duration may occasionally be three or even 10 days, but generally it is either five or seven days—though there is no reason to believe that seven days is ever better than five. A study that we have conducted indicates the confusion surrounding this issue and the cost of the two extra days' treatment.

We obtained data from the Prescription Pricing Authority for 1992-3 for all prescriptions for tablets or capsules of amoxycillin, ampicillin, cephalaxin, and erythromycin at 250 mg and 500 mg strengths (omitting ethinyl succinate erythromycins); phenoxymethylpenicillin 250 mg; trimethoprim 200 mg; and co-trimoxazole 400/80 mg. We analysed only items prescribed for short durations and categorised them as five day, seven day, or other by applying standard dosage-frequency to the size of the item: 21 and 15 capsules were commonest for amoxycillin 250 mg, and we took these as seven and five day courses respectively.

Nationally, 36.8% of courses were for five days (5 149 001/13 973 878) and 47.1% for seven days (6 576 613/13 973 878). Only for phenoxymethylpenicillin did five day courses clearly exceed seven day courses, though for ampicillin the split was roughly even. There was great variation among regions (with five day courses predominating in South Western and Wessex) and among family health services authorities.

To look at variation among doctors we studied singlehanded practices and excluded items known to have been given by deputies, locums, and trainees. For 1817 practices there were 816 062 items, with seven day courses again more common except in the case of phenoxymethylpenicillin. Analysis of the 11 preparations combined showed that most practices used both durations of courses, but for the individual preparations there was considerable polarisation. Doctors varied the duration according to which antibiotic they gave but differed over which antibiotic should have which duration. Doctors in partnerships probably behave like their singlehanded colleagues in this respect.

Nationally the cost of the extra two days'

treatment lay between £1.9m and £7.2m, depending on whether it was calculated on the basis of generic or brand leader prices. Had we included the liquid formulations and every other antibiotic, the cost would have been much higher. Some antibiotics are packaged as seven day courses, and this encourages doctors to waste money; original pack dispensing is likely to result in even more waste.

CONRAD M HARRIS
Director
DAVID C E F LLOYD
Applied statistical officer

Prescribing Research Unit,
University of Leeds,
Leeds LS2 9NZ

Adult epiglottitis

Cefuroxime is effective

EDITOR,—Jonathan H Raphael comments on the likely aetiology and antibiotic treatment of epiglottitis in adults.¹ He describes a case caused by *Streptococcus pyogenes* in which improvement occurred only after benzylpenicillin was added to cefuroxime. The organism "proved sensitive to benzylpenicillin but resistant to cefuroxime." While no one would question that benzylpenicillin is the antibiotic of choice for serious infections due to *S pyogenes*, the author does not make clear whether he is describing clinical or microbiological failure with cefuroxime; the two are very different. He does not mention antibiotic doses to permit comment on clinical failure. Nor does he state how it was decided that the organism was resistant to cefuroxime. *S pyogenes* is exquisitely sensitive in vitro to both benzylpenicillin and cefuroxime, with minimum inhibitory concentrations of the order of 0.007 and 0.06 mg/l respectively. The recommended breakpoint minimum inhibitory concentration for cefuroxime is 4 mg/l.² If the minimum inhibitory concentration of this isolate is considerably higher than the figures quoted here then it is of great interest to microbiologists and clinicians.

Empirical treatment of any serious infection must cover the most likely pathogens. Cefuroxime would provide that cover in adult epiglottitis. Once an organism has been isolated, treatment may need to be changed to the most appropriate antibiotic for that organism. Clinical failures can occur with any antibiotic but must be distinguished from in vitro resistance.

KEITH F BARKER
Consultant microbiologist
BHARAT PATEL
Senior registrar, microbiology

Public Health Laboratory and Department of Microbiology,
Central Middlesex Hospital NHS Trust,
London NW10 7NS

1 Raphael JH. Adult epiglottitis. *BMJ* 1994;308:719. (12 March.)

2 British Society for Antimicrobial Chemotherapy. A guide to sensitivity testing. *J Antimicrob Chemother* 1991;27(suppl D).

Seek microbiological advice

EDITOR,—I was both surprised and dismayed to read the brief case report presented by Jonathan H Raphael.¹ My surprise related to his erroneous microbiological statement and my dismay to the lack of consultation with the local microbiology laboratory before publication of his letter.

Any microbiologist would recognise that β haemolytic streptococci group A are sensitive to both cefuroxime and benzylpenicillin and would not report them as resistant to cefuroxime. The argument that antibiotics effective against *Haemophilus influenzae* are insufficient in adult epiglottitis is therefore incorrect and not supported in this case. Serious sepsis, such as epiglottitis in an adult, should ideally be managed in consultation with a microbiologist. Any publication including

microbiological data and their interpretation should also involve the microbiologist.

ANDREW SWANN
Consultant microbiologist

Joint NHS/PHLS Microbiology Laboratory,
Leicester Royal Infirmary,
Leicester LE1 5WW

1 Raphael JH. Adult epiglottitis. *BMJ* 1994;308:719. (12 March.)

Reye's syndrome

EDITOR,—We agree with John F T Glasgow and Raymond Moore that Reye's syndrome is a heterogeneous disorder.¹ Indeed, it is a non-specific clinicopathological entity, the microvesicular lipid accumulations evident in the liver on light microscopy now being considered to be a non-specific finding for which there are many other causes.^{1,2} Electron microscopy is now recommended, but in the epidemiological studies reported it has been done in relatively few cases. With regard to aetiology, it is clear that the diagnosis of Reye's syndrome has been revised recently in favour of an inherited metabolic disorder in many patients; other patients are nowadays more correctly diagnosed as having viral disease or an escalation of symptoms induced by antiemetics, whose side effects are now better recognised.²

This improved diagnosis, however, implies that the American and British epidemiological studies that suggested a link between Reye's syndrome and aspirin were done on a heterogeneous group of children with different diseases. This fact alone weakens their hypothesis. In the studies carried out by the Centers for Disease Control only the drugs used before the onset of severe vomiting were registered; thus drugs—for example, antiemetics—given between the onset of vomiting and admission to hospital were excluded. Moreover, the Ohio survey first started by registering all drugs taken throughout the illness, but when these data indicated that not only the use of aspirin but also that of phenothiazines and trimethoprim hydrochloride was significantly greater in cases of Reye's syndrome than controls the questionnaire was revised.³ Only the drugs given before the onset of vomiting were then registered, and thus the same bias was introduced as in the other surveys.

Defining the day of onset of severe vomiting as the onset of Reye's syndrome is arbitrary and results in incorrect data on use of drugs. This arbitrary definition is the key to the whole theory. Indeed, there is no proof that vomiting reflects the early stages of cerebral oedema or the onset of Reye's syndrome; vomiting is often a symptom inherent to the viral infection.² And in some patients the "encephalopathy" was misleading extrapyramidal reactions induced by antiemetics.²

In the British risk factor study the use of antiemetics was significantly higher in patients with Reye's syndrome than in the comparison group.⁴ Indeed, of 106 patients with Reye's syndrome, 33 had taken at least one antiemetic or antihistamine, or both, before admission compared with 17 of the 185 control patients ($P < 0.0001$); of these, 15 patients with Reye's syndrome versus three controls had taken an antiemetic such as metoclopramide ($P = 0.0001$).⁵ (S Hall, personal communication). The British data and the analysis of the Ohio study² show that not only the use of aspirin but also the use of antiemetics, phenothiazines, or other antihistamines is significantly greater in cases than controls.

Why then do people repeat that the only link is the one between aspirin and Reye's syndrome? Would it not be more logical to point to the antiemetics known to be neurotoxic? Their possible role was suggested by the Food and Drug Administration in 1976.⁵ The apparent decline of Reye's syndrome is not a factor in favour of a link with aspirin as increased recognition of metabolic,

viral, or toxic diseases may explain this "pseudo decline."^{1,2} In conclusion, Reye's syndrome should be reassessed.

MARIA CASTEELS-VAN DAELE
EPHREM EGGERMONT

Department of Paediatrics,
University Hospital Gasthuisberg,
University of Leuven,
3000 Leuven, Belgium

- 1 Glasgow JFT, Moore R. Reye's syndrome 30 years on. *BMJ* 1993;307:950-1. (16 October.)
- 2 Casteels-Van Daele M. Rye syndrome or side-effects of anti-emetics? *Eur J Pediatr* 1991;150:456-9.
- 3 Halpin TH, Holtzauer FJ, Campbell RJ, Hall LJ, Correa-Villaseñor A, Lanese R, *et al.* Reye's syndrome and medication use. *JAMA* 1982;248:687-91.
- 4 Hall SM, Plaster PA, Glasgow JFT, Hancock P. Preadmission antipyretics in Reye's syndrome. *Arch Dis Child* 1988;63:857-66.
- 5 FDA's Neurologic Drugs Advisory Committee. Reye's syndrome: etiology uncertain, but avoid antiemetics in children. *FDA Bulletin* 1976 Nov-Dec:40.

Water births given a bad press

EDITOR,—The response of the Royal College of Obstetricians and Gynaecologists to questions on the safety of water birth and the resulting widespread publicity generated last year, raise issues that should concern all health care professionals.

Water birth is a new technique that needs to be properly tested for effectiveness, efficiency, and safety. Although some obstetric interventions in the past were introduced without evaluation, the introduction of water birth has been cautious and well documented, and the technique is currently under study. The John Radcliffe Hospital in Oxford is halfway through a three year study to assess the outcome in women using a water pool. Initial published results give details of the 300 women who used the pool between August 1990 and August 1991.¹ More than 600 women have now used the pool during labour, and over 300 of them have given birth under water. In addition, the Department of Health has sponsored the National Perinatal Epidemiology Unit to collect and evaluate data on the use of water birth throughout the country.

This must be the proper way to proceed. Until these studies and trials are completed no one can judge the effectiveness or safety of the procedure. By drawing attention to water birth in the way in which it did, however, the Royal College of Obstetricians and Gynaecologists may have jeopardised the success of these clinical studies. Some women may well withdraw from the trials. The Royal College of Midwives has supported the cautiousness of the advocates of water birth. We agree that many women find being in water comforting during labour, but we realise that there is much yet to be learnt. The use of studies, trials, and audit seems wholly responsible.

A further point is the naivety of some professionals in their dealings with the media. News values being what they are, it should have been obvious that there would be little attempt to balance views on the safety of water birth. Without the hysteria, the popular press would not have had a story at all. The passing of opinion and conjecture as established medical fact caused many women, midwives, and obstetricians needless anxiety.

The way to deal with controversial new procedures is through multiprofessional debate, research, rigorous audit, and consensus. To cause distress on the basis of so little evidence and to put at risk the current research which is hoped will give that evidence seem to be wholly irresponsible.

ROSEMARY JENKINS
SUZANNE TYLER

Royal College of Midwives Trust,
London W1M 0BE

- 1 Burns E, Greenish K. Pooling information. *Nursing Times* 1993 Feb 24:47-9.

Chemotherapy in advanced small cell lung cancer

EDITOR,—I E Smith argues that there is good evidence for the place of chemotherapy in controlling symptoms and prolonging survival in advanced non-small cell lung cancer.¹ Smith's argument is largely based on comparison of the data available with data on other "standard" treatments. Simply to assert that the evidence supporting the use of chemotherapy in advanced non-small cell lung cancer is as good as that for using palliative radiotherapy in the same disease² or chemotherapy in advanced breast cancer is hardly persuasive. Neither of these could be described as thoroughly studied cancer treatments, and neither is notably successful.

The survival data referred to³ also fall short of being conclusive since they are derived from an overview of published trials. In such overviews and meta-analyses trials with different entry criteria and treatment regimens are amalgamated. It is well known that they may be influenced by a positive publication bias in favour of "good results." Finally, the evidence of an impact on patients' symptoms is taken from a small non-randomised study in a single institution.

In the historical development of new treatments there is often a relatively narrow time window in which to accumulate comprehensive, reliable information on the impact of treatment. Fashion and the understandable desire to offer some treatment where previously there was none can overtake scientific endeavour. Evidence of a treatment effect, such as the response rate, is not sufficient to justify recommendation of a treatment in a journal such as the *BMJ* with a worldwide influence.

We are currently running randomised controlled trials of chemotherapy (mitomycin, ifosfamide, and cisplatin⁴) in inoperable non-small cell lung cancer with survival as well as quality of life end points. Over 600 patients have been randomised, with a target of 800. These two trials (one in localised and one in advanced disease) will provide more definite information that will allow oncologists to make informed judgments concerning the place of this treatment among other priorities in health care systems with limited resources. We urge Smith and others to help us by collaborating in this work.

DAVID R FERRY
MICHAEL H CULLEN

Birmingham Oncology Centre,
University of Birmingham,
Queen Elizabeth Hospital,
Birmingham B15 2TH

- 1 Smith IE. Palliative chemotherapy for advanced small cell lung cancer. *BMJ* 1994;308:429-30. (12 February.)
- 2 Lung Cancer Working Party of the Medical Research Council. Inoperable non-small cell lung cancer: a Medical Research Council randomised trial of palliative radiotherapy with two or ten fractions. *Br J Cancer* 1991;63:265-70.
- 3 Souquet PJ, Chauvin F, Boissel JP. Polychemotherapy of advanced non-small cell lung cancer. *Lancet* 1993;342:19-21.
- 4 Cullen MH, Chetiwardana AD, Joshi R, Woodroffe CM. Mitomycin, ifosfamide and cisplatin in non-small cell lung cancer: treatment good enough to compare. *Br J Cancer* 1988;58:359-61.

GP facilitators and HIV infection

EDITOR,—Peter Saunders¹ and subsequent correspondents² raise many issues relevant to general practitioner facilitators and HIV infection in Lothian. Of 1000 adults known to have HIV infection in Lothian, 60% have acquired HIV through needle sharing, but for the past three years heterosexual transmission has been the commonest mode of spread. At the suggestion of a group of interested general practitioners, Lothian Health Board established a facilitator team in 1989. In

1992 it was expanded to three part time staff: a working general practitioner, a retired general practitioner, and a retired health visitor.³ The nurse facilitator concentrates on non-medical members of the primary care team, focusing on issues of HIV prevention, while the medical facilitators support general practitioners to care for drug users and for people with HIV infection. We work closely with hospitals and non-statutory agencies, and the emphasis has been on supporting primary care teams in their care of people with HIV infection rather than on asking them to do more at a time of increasing demands on general practice.

We circulate regular information sheets to general practitioners, organise courses for doctors and nurses, and visit practices to provide information, training, and support to all members of the practice team.³ We have developed teaching aids and resources (such as a leaflet and a combined pill and condom pack) to support general practitioners and primary care nurses in their prevention work and have been involved in auditing the quality of community care for people with HIV infection.⁴ In 1991 and 1993 a 99% response to a survey of all practices in Lothian provided a detailed picture of the epidemiology of HIV infection and drug use in Lothian general practice.⁵ By 1993, 70% of the 133 practices in Lothian as a whole—including 93% of the 76 practices in the city of Edinburgh—had experience of patients with HIV infection. Only four practices were caring for more than 20 people with HIV infection, and most practices (46%) had between one and five patients with HIV infection.⁵

We share with Singh *et al*⁶ an interest in evaluating the work of facilitators, and from the team's inception we have consistently evaluated individual activities.³ As for the wider impact of facilitation, we have been unable to distinguish this from the effects of the Lothian approach to HIV care in general. We can, however, point to the increasing involvement of Lothian general practitioners in shared care and the continuing goodwill associated with facilitator activities, of which the remarkable response rate to our epidemiological survey is an example.

JUDY BURY
MURIEL SIMMONTE
SARAH COWPER
Primary care facilitator team
(HIV/AIDS and drugs)

Spittal Street Centre,
Edinburgh EH3 9DU

- 1 Saunders P. GP facilitators and HIV infection. *BMJ* 1994;308:2-3. (1 January.)
- 2 Correspondence. GP facilitators and HIV infection. *BMJ* 1994;308:538-9. (19 February.)
- 3 Bury J. *The primary care facilitator team: report on the first four years.* Edinburgh: Lothian Health, 1994.
- 4 Huby G, van Teijlingen E, Porter M, Bury J. *A study of discharges from hospital into the community of people with HIV infection.* Edinburgh: University of Edinburgh Department of General Practice, 1994.
- 5 Bury J. *HIV infection and drug misuse in Lothian general practice: report on epidemiological questionnaire 1993.* Edinburgh: Lothian Health, 1994.

Bias in assignment to clinical trials

EDITOR,—Despite the many biases to which clinical trials are subject, trials are still considered the best way to show the efficacy of a new therapeutic or prophylactic measure.¹ Perhaps the most important biases are those of selection and measurement, as they most determine the validity of a study. The respective techniques of random assignment to study treatment groups and of blind experimentation are attempts to remove these biases.

We have detected a type of selection bias that does not affect the assignment of subjects in a single study to different groups but rather the