and 413 non-insulin dependent diabetics whose duration of diabetes ranged from 0.5 to 40 years. Urinary albumin was measured by rocket electrophoresis. For our normal range we measured albumin to creatinine ratios in 250 non-diabetic healthy volunteers (mean 0.75 (SD 0.93)). The upper limit of normal was defined as 2.6 (mean + 2SD). Twenty per cent of the results obtained from insulin dependent diabetics and 25% of those from non-insulin dependent diabetics were positive. Interestingly 19% of both groups were found to be positive within two years of diagnosis. Repeat sampling on at least three occasions showed, however, that positive results were far from consistent. Results were considered to be true positives if there were three consecutive positive results; transient positives occurred when a positive result was followed by negative results. True negatives occurred when there were three negative results, and transient negatives occurred when there was a single negative result with at least two positive results. On this classification and assuming that the patients with true positive results represent those more likely to develop macroalbuminuria and renal failure, then 6.6% of insulin dependent diabetics and 13% of non-insulin dependent diabetics were at risk after two years. When true positive and transient negative results were combined then 13% and 23% respectively showed positive values.

These studies emphasise the high proportion of transient positive results (21% in insulin dependent and 19% in non-insulin dependent diabetics), and we strongly recommend that at least three samples should be tested over several weeks to confirm truly positive microalbuminuria. Whether "transient" negative microalbuminuria is of any importance must remain more speculative.

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Collars and corsets

SIR,—We are concerned at the implication in Dr G J Huston's article (23 January, p 276) that physiotherapy is a physical placebo in the treatment of neck problems, especially those resulting from road traffic accidents.

The main reference used by the author in coming to the conclusion that "soft collars may be a less expensive means of providing a physical placebo than physiotherapy" is concerned mainly with acute nerve root problems rather than those associated with road traffic accidents and was published 20 years ago.¹

While a regimen of early treatment of whiplash injuries by ice and heat, Maitland mobilisations, and hourly exercises within pain limits as advocated by Mealy *et al* appears to be a more expensive option, their study showed a significantly greater improvement in cervical movement and decrease in intensity of pain at eight weeks.²

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- 1 British Association of Physical Medicine. Pain in the neck and arm: a multicentre trial of the effects of physiotherapy. *Br Med J* 1966;i:253-8.
- 2 Mealy K, Brennan H, Fenelon GCC. Early mobilisation of acute whiplash injuries. *Br Med J* 1986;292:656-7.

SIR,—Dr G J Huston (23 January, p 276) concluded that collars and corsets acted as a less expensive

physical placebo than physiotherapy, which itself is unstudied.

The references he used were rather out of date (1957 and 1966). I would refer him to more recent works, such as those of Mealy *et al* and of Kopp *et al*.¹ Both of these papers, with others, refute the placebo effect of physiotherapy theory put forward by Dr Huston.

On the question of fitting corsets, this is frequently done by physiotherapists as there are often no orthotists available. It is a great pity that these outmoded statements are allowed to be perpetuated as they do nothing for the relationship between chartered physiotherapists and doctors.

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- 1 Kopp JR, Alexander AH, Turocy RH, *et al*. The use of lumbar extension in the evaluation and treatment of patients with acute herniated nucleus pulposus: a preliminary report. *Clin Orthop* 1986;202:211-8.

AUTHOR'S REPLY.—I am grateful for the opportunity to expand on a very brief article. The trial of treatment of neck and arm pain quoted in my review is large and has not been superseded. The predominantly female population described, who had pain in the neck, shoulder, and arm and were mostly aged between 40 and 60 years, is typical of the patients encountered in a rheumatology clinic and clearly a different population from the young predominantly male group attending an accident and emergency department after whiplash injury, as described by Mealy *et al*. This latter study, while it must be a great encouragement to physiotherapists to progress to further research, described two groups each given a number of treatments. It is impossible to tell whether home exercises (cheap) or manipulative physiotherapy (expensive) contributed to the improvement described in one of these groups. This study cannot therefore be used to support the application of manipulative physiotherapy in patients with non-traumatic neck pain.

I maintain that the cost effectiveness of manipulative physiotherapy in the treatment of neck pain remains an unstudied area.

I will be as delighted as every other physician when an effective treatment for neck pain is defined. Until then I must rely on explanation and encouragement with or without unproved and placebo therapies. I suspect that placebos currently used may perform relatively well if examined for improvement in quality of life per unit cost. I hope that the Chartered Society of Physiotherapy will be able in a few years to define effective treatments for neck pain in different populations as a result of studies stimulated by its members. Such studies would do much for the relationship between chartered physiotherapists and doctors.

I am surprised that the greater part of fitting of corsets is performed by physiotherapists but grateful to Ms Little for this information, as I found it impossible to discover from the DHSS even the gross number of corsets fitted annually in Britain.

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Pancreatic cancer

SIR,—Professor R C N Williamson (13 February, p 445) has highlighted the depressing realities of treating pancreatic cancer. The long term goals are

elucidating the aetiology of the disease and refining diagnostic techniques to detect early lesions. Nevertheless, there are approaches that are worth exploring now.

Tamoxifen is unlikely to have an important impact on outcome.¹ In contrast, there have been two recent and potentially important studies from the North American Gastrointestinal Tumour Study Group. In the first study 43 patients who had had resection of their cancers were randomised to a control group or a treatment group, which received two 2000 rad (20 Gy) courses of supervoltage radiation after surgery and fluorouracil weekly for two years.² This regimen was repeated in a second cohort of 30 patients.³ The two year survival was 43% and 46% respectively in these treated groups with a probable 20% five year survival. These results are superior to anything previously reported.

There may be even better regimens of potential value, but it is vital that the efficacy of this one is assessed. We are about to launch a national study of postoperative radiotherapy and fluorouracil coordinated by the West Midlands Cancer Research Campaign clinical trials unit. We would welcome the participation of all interested surgical and oncological units.

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- 1 Crowson MC, Dorrell A, Rolfe EB, Fielding JWL. A phase II study to evaluate tamoxifen in pancreatic adenocarcinoma. *Eur J Surg Oncol* 1986;12:335-6.
- 2 Gastrointestinal Tumour Study Group. Adjuvant combined radiation and chemotherapy following curative resection. *Arch Surg* 1985;120:899-903.
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Complications of erythema infectiosum in pregnancy

SIR,—Dr P K Buxton (23 January, p 257) mentions that the main complication of rubella is congenital abnormalities in infants of women exposed to rubella during pregnancy. He then discusses erythema infectiosum or fifth disease, caused by parvovirus B19, which, he states, has no reported complications. This, however, is at variance with the experience of obstetricians and virologists. There is now extensive evidence that human parvovirus B19 infection is associated with spontaneous abortions in the first trimester,¹ hydrops fetalis resulting in intrauterine death in the second trimester,² and stillbirth at term.³

Parvovirus attacks the fetal haematopoietic system, destroying the host cell. The resulting haemolysis and leucoerythroblastic anaemia will cause cardiac failure, oedema, and ascites similar to those seen in severe rhesus disease and will result in intrauterine death. Maternal infection in pregnancy does not consistently produce fetal problems; the full extent of fetal infection is unknown, but it appears to complicate about one third of maternal infections during pregnancy.^{1,2} Like rubella and cytomegalovirus, subclinical maternal parvovirus infection does not exclude the possibility of intrauterine infection. Raised maternal serum α foeto-protein concentrations in the second trimester in pregnancies complicated by parvovirus infection may act as a marker of fetal infection and poor fetal prognosis in advance of ultrasonic detection of fetal hydrops.⁴ The fetal leucoerythroblastic anaemia can also be diagnosed by fetal blood sampling.⁴

Parvovirus infection is also not without com-

plications in adults, in whom it has been associated with a seronegative arthropathy,⁵ which may or may not be accompanied by a rash. It may also produce aplastic crises in patients with chronic haemolytic anaemias such as hereditary spherocytosis and sickle cell disease.⁶

Practitioners concerned in antenatal care should therefore be alert to the possibility of parvovirus infection and its possible complications. Women complaining of a rash or arthropathy during pregnancy or who are in contact with a child with erythema infectiosum should be screened serologically for parvovirus infection. If infection is confirmed the fetus should be monitored by maternal serum α fetoprotein concentrations, which may predict fetal infection, and by ultrasound to detect fetal hydrops. Fetal blood sampling may also be of value in diagnosing fetal anaemia. Parvovirus is an appreciable cause of non-immune fetal hydrops and resultant fetal loss and women at risk should be screened for evidence of infections during pregnancy.

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- 1 Mortimer PP, Cohen BJ, Buckley MM, *et al*. Human parvovirus and the fetus. *Lancet* 1985;iii:1012.
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Cough and angiotensin converting enzyme inhibitors

SIR,—For Dr Christine Bucknall and others (9 January, p 86) to say that cough associated with converting enzyme inhibitors may be a variant of the cough in asthma may cloud the issue of the pathogenesis of this adverse reaction. Our epidemiological data and the observations of others show that there is a significant preponderance of women in reports of cough with captopril and enalapril.¹⁻³ There is, however, no such sex difference with asthma, which suggests that the mechanism of production of cough with asthma and that with converting enzyme inhibitors are different. Unfortunately, the authors' study did not match controls and cases for sex, three of eight cases and six of nine controls being men.

The question of an association of angiotensin converting enzyme inhibitors with an asthma wheeze is interesting. Dr Bucknall and colleagues included in their study two patients with bronchial asthma who had reported increased wheeze after treatment with enalapril. These patients showed poor control of their asthma before the start of the rechallenge protocol, which started six and 12 weeks after they had stopped taking enalapril, and inhaled steroids had been introduced to control the increased wheeze. Our observations with the cough reaction were that symptoms cleared rapidly on withdrawal, the mean recovery time being 3.4 days for captopril and 5.5 days for enalapril.¹ These facts would suggest that either the exacerbation of wheeze and the cough reaction were produced by different mechanisms or the wheeze was not a reaction and represented a natural progression of bronchial asthma.

We are not convinced that angiotensin convert-

ing enzyme inhibitors include among their reactions exacerbation of bronchial asthma. The number of reports of cough so far received at this centre is 167, but we have only eight reports of wheeze or exacerbation of asthma, and we have described three asthmatic patients with cough but no increase in wheeze.¹ One study of seven patients with a cough attributable to converting enzyme inhibitors failed to show either reversible airflow obstruction or altered bronchial reactivity to methacholine.⁴ Prostaglandins might have a role in the pathogenesis of the cough reaction,¹ and the observation that sulindac can clear or reduce the cough suggests that their contribution is a major one.⁵ This again highlights the difference from bronchial asthma, which is not alleviated by non-steroidal anti-inflammatory drugs.

The incidence of a cough reaction is difficult to assess. Retrospective analyses of highly selected groups of patients—for example, those attending hypertension clinics—could produce an artificially high incidence. The incidence observed by us of 1.1% for captopril and 2.8% for enalapril¹ is probably low because these were reported cases only, but the patient population was unselected and we believe the monitoring method used revealed most clinically important cases. The incidence of cough is probably close to these figures.

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- 1 Coulter DM, Edwards IR. Cough associated with captopril and enalapril. *Br Med J* 1987;294:1521-3.
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Skin reactions and fever with indapamide

SIR,—We appreciate the interest that Drs D Kandela and D Guez (20 February, p 573) have shown in our short report (21 November, p 1313), but we find their letter misleading.

Our paper was a reviewed article and also follows the guidelines formulated by a workshop held under the auspices of Ciba-Geigy.¹ Unfortunately the references of skin reactions to indapamide that they mention do not satisfy these criteria. Even so, we wonder why they did not include them in their product datasheet.

Although we clearly stated that our figures were based on data obtained by voluntary reporting, and that no conclusions could be drawn about the comparative incidence of adverse effects to the different drugs mentioned in the article, Drs Kandela and Guez have wrongly understood that it was our purpose to do so. Their statement about the "highly comparable absolute numbers of cases: 16 and 15 respectively" (of skin reactions to indapamide and chlorthalidone) is irrelevant: chlorthalidone is more widely used in The Netherlands than indapamide, and the relative number of skin reactions to indapamide was much higher than that to chlorthalidone. The same applies to their interpretation of the figures on (hydro)chlorothiazide and frusemide. There is no logic in comparing absolute numbers without comparing prescription figures, and we have some difficulties in understanding their concept "absolute incidence."

Our conclusion that indapamide can cause skin

reactions, sometimes serious, still holds, and these reactions were not mentioned in the datasheet. (The reporting of skin reactions to indapamide has increased considerably during the past year, and the World Health Organisation database now holds 266 such reports.)

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HIV, hepatitis B, and sexual behaviour

SIR,—The report by Dr Brian A Evans and others (13 February, p 473) raises disturbing ethical issues, and I was surprised to see no reference to these. Screening for antibodies to the human immunodeficiency virus (HIV) has been the subject of much debate both in your journal and elsewhere.

They state that 1115 women were included in their study and that all were offered the opportunity to ask for an HIV antibody test; 207 accepted the offer, but this means that 908 did not. Surely this means that they were implicitly refusing consent for the test. Despite this the test was carried out on all women.

While the screening test was carried out "independently of and separate from the clinical records," the results were clearly traceable to individual patients as in the case of the one positive result they obtained. This patient was then again counselled. It is difficult to see how they explained this repeat counselling to her, alone of 1115 women, without raising anxiety that there was something wrong. The counsellor presumably knew the result of the first test and would have been encouraging the patient to be tested. Despite this she explicitly declined the test.

Thus the doctors were left with a highly important test result for which permission had been refused. What are they then to do with the result? It has been connected to her case notes. How can the patient be protected from accidental revelation of the result in the future? Is it ethical to withhold the information from the patient when it is critically important to her sexual and reproductive behaviour and her subsequent clinical management?

These impossible dilemmas could have been avoided if patients had not been tested when consent had been withheld.

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SIR,—Dr Brian A Evans and colleagues indicate a low prevalence of antibodies to the human immunodeficiency virus (HIV) in a large cohort of heterosexual women attending a sexually transmitted disease clinic in London. This may at first be reassuring, and the authors conclude that heterosexual women are at low risk in London, but the risk of drawing this conclusion from inadequate, or at times absent, information is perilous.

Those women who were found to be infected were sexual contacts of high risk individuals, and the reasonable conclusion must be that the majority who remained uninfected had sexual partners who were not infected. Transmission was not shown because there was no risk. All this study shows, therefore, is a low prevalence in intravenous drug users and bisexual men—and we know this