relationship between the extent of husbands' smoking and lung-cancer risk of non-smoking wives by a case-control study. The results clearly confirmed my findings generated from a large-scale cohort study.

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Successful plasmapheresis in the Miller-Fisher syndrome

SIR,—Since the original report[1] several centres have reported rapid recovery from idiopathic inflammatory polyneuropathy with plasma exchange. It is therefore very important that negative results should also be documented, such as the two cases described by Dr D N Maisey and Dr S A Olczak (4 April, p 1159). It is also important, however, that comparable modes of treatment should be used, and in these two cases failure to respond may well have been due to "too little too late."

In our experience,[1 2] acute cases that have improved were exchanged early in the course of the illness. In Maisey and Olczak's first case the patient had been on a ventilator for six weeks before treatment was started. Furthermore, this patient had a total of 6·9 l exchanged over five days, and the second patient only 3 l over two days. These volumes are small compared with those used by other operators for the same disease and in other disease processes,[3] particularly if the figures given do not allow for priming solution and heparin infusion. Exchanges of 40-55 ml/kg (3-4 l) daily for at least four days are needed to remove 95% of any intravascular factor per exchange and 90% of total body immunoglobulin all told.[4]

Cases of inflammatory polyneuropathy probably constitute a heterogeneous group, and it would be surprising if every patient proved to benefit from plasma exchange. The difficulty is knowing who might improve. So far none of our patients has deteriorated, and this is reassuring.

We agree that a formal multicentre clinical trial is necessary, and, indeed, such a trial has already been started in the United Kingdom. In experienced hands plasma exchange is not a complex procedure. It is time-consuming but relatively simple, and cell separators are already available in many hospitals for other purposes. The cost can be reduced by using cheaper replacement solutions, and we are at present evaluating how little plasma protein fraction is really necessary.

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SIR,—You have recently published two reports concerning "plasmapheresis," a short report from Drs Ross Littlewood and Serge Bajada (7 March, p 778), or "plasma exchange," a letter from Drs D N Maisey and S A Olczak (4 April, p 1159). These terms are, unfortunately, regarded by many authors as synonymous; however, used correctly they define quite different procedures with differing short- and long-term effects on plasma constitution (as well as different hazards).[1] In plasmaph(a)eresis (αφαιρεσιδ =a taking away) plasma is removed—either without volume replacement or with crystalloid alone. Plasma exchange involves exchange of the patients' plasma for plasma or plasma fractions; different fractions (plasma protein fraction ≙ albumin; fresh frozen plasma ≙albumin and globulins) may have quite different effects on plasma proteins and on clinical response.[2]

Neither of the two recent reports specify the replacement solution used (if any); and other details of the procedures are sketchy. Without this essential information such publications are of limited value, either scientifically or clinically. Plasma exchange (or plasmapheresis) is analogous to a class of drugs; clinical reports should give the name of the specific agent, the dose and mode of administration, together with any concurrent therapy. Precision in published reports can help to minimise wastage of blood products and of human and financial resources.

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Comparison of oestradiol and prostaglandin E_2 vaginal gel for ripening the unfavourable cervix

SIR,—I was interested to read the report by Mr Philip Tromans and others (28 February, p 679), describing the similar effects on cervical "ripening" of oestradiol and prostaglandin E_2 (PGE_2). Their observation of the inadvertent, and at times potentially hazardous, induction of labour in the prostaglandin group is certainly confirmed by clinical experience and raises the question of the underlying mechanisms involved in the changes seen.

We have been investigating the role of proteases in collagen breakdown in the cervix during pregnancy, and have recently reported a highly significant increase in the activity of a specific peptidase, PZ (4-phenylazobenzyl-oxycarbonyl) peptidase, in the pregnant cervix both before and after labour.[1] We have also assessed the effect of various substances on the activity of the enzyme, and may thus be able to suggest a mechanism for the observed changes in cervical compliance, traditionally considered to be the result of subclinical uterine activity.

PGE_2, 17β-oestradiol, and oxytocin were added to the substrate tissue-homogenate mixture during incubation to assess PZ peptidase activity. Graded final concentrations from 10^{-6} to 10^{-14} mg/ml, from 10^{-5} to 10^{-8} mol/l, and from 5 to 50 mU/ml respectively were used. None of these substances had a significant effect on the rate of substrate breakdown. Earlier work by Hillier *et al*[2] demonstrated an increase in hydroxyproline production, this being indicative of collagen breakdown, when PGE_2 and oestradiol in similar concentrations were added to short-term tissue cultures of non-pregnant cervix. We are at present undertaking similar work on pregnant tissue. These results suggest the prostaglandin and oestradiol have no direct effect on enzymatic breakdown of collagen, but that enzyme production may be increased.

We have also looked at the effect on activity of acetyl salicylate, as a prostaglandin-synthetase inhibitor, in final concentrations of 0·5-20 μg/ml. A significant depressant effect ($p<0.01$) was seen whether the substance was added to the incubation mixture or immediately after collection, demonstrating a direct inhibitory effect. Mean rates of substrate breakdown (nmol/min mg protein) in a group of 10 samples were 0·40±0·15 without salicylate, 0·24±0·10 at 5 μg/ml, and 0·15±0·09 at 20 μg/ml. These results are in agreement with the clinical observation of cervical dystocia after the administration of prostaglandin synthetase inhibitors.

It is thus possible in theory, as well as in practice as demonstrated by Mr Tromans and his colleagues, that mechanisms exist which will allow the manipulation of cervical compliance by inducing biochemical change in the cervix. This may occur independently of uterine activity. The unpredictable and thus potentially hazardous effect of prostaglandin administration producing uterine contractions, when the intention was to induce cervical softening, may therefore possibly be avoided by the understanding of the mechanisms normally concerned with this change.

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SIR,—I was most interested in the results reported by Mr Philip M Tromans and his colleagues (28 February, p 679) comparing the ability of oestradiol and prostaglandin E_2 to ripen the unfavourable cervix before induction of labour.

Following work with Dr A A Calder on the ripening effect of oestradiol on the unfavourable cervix,[1] I compared the effect of oestradiol (150 mg in 6 ml hydroxyethylmethylcellulose gel) with that of prostaglandin E_2 (400 μg in 6 ml hydroxyethylmethylcellulose gel). There were 25 primigravidas in each group with cervical scores of 3 or less, and the treatment was given extra-amniotically the night before planned induction. There were no significant differences in the maternal age, height, weight, or length of gestation and all patients had a singleton cephalic presentation. The results are shown in the accompanying table.

The indications for caesarean section were cephalopelvic disproportion in both patients in the PGE_2 group and fetal distress in two cases, and failure to progress in the oestradiol group. The only statistically significant difference between the two groups was in the

Comparison of treatment with oestradiol and prostaglandin E_2

	PGE_2 group (n=25)	Oestradiol group (n=25)
Mean cervical score at priming (±1 SD)	2·1±0·7	2·3±0·6
Spontaneous onset of labour	48% (12)	4% (1)
Mean cervical score at induction (±1 SD)	5·5±1·1	5·5±1·1
Mean duration of labour in hours (±1 SD)	9·8±3·5	10·5±3·6
Mean Apgar score at one minute (±1 SD)	7·8±1·4	7·9±1·6
Patients requiring ceasarean section	8% (2)	12% (3)