factors, including developmental and genetic, may underlie panacinar emphysema, which sometimes affects coal workers and becomes pigmented. Acquired fibrocystic disease, which in coal workers is often heavily pigmented, must also be distinguished from emphysema. On present evidence it is difficult to envisage a primary role for alveolar macrophages in the genesis of emphysema. Even in α_1 -antitrypsin deficiency, an uncommon state in which leucocytic protease activity may be directed against connective tissue, other factors may co-operate in the genesis of emphysema. The occurrence of alveolar fenestrae and capillary damage may merely represent the early stages of secondary non-specific disruption, which when advanced and widespread and possibly complicated by infection renders it difficult to assess the relative significance of the different pathogenetic processes in emphysema.—I am, etc.,

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- ¹ Heppleston, A. G., *Annals of the New York Academy of Sciences*, 1972, **200**, 347.
² Ryder, R. C., Dunnill, M. S., and Anderson, J. A., *Journal of Pathology*, 1971, **104**, 59.

Psychiatry in the Soviet Union

SIR,—Dr. G. Morozov offers us evidence (6 July, p. 40) of the objectiveness of Soviet forensic psychiatry by referring to five dissidents whose mental illness was confirmed by an international team of psychiatrists. We must accept that judgement with respect. Unfortunately, as we are not told how or by whom these five patients were selected it proves nothing about the diagnosis made on other dissidents. Consequently it cannot refute in any way the complaints from distinguished Soviet citizens that many dissidents are still being interned in mental hospitals purely on account of their dissent.—I am, etc.,

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Sex for Medical Students

SIR,—Dr. Ronald Fletcher's analysis of the problems surrounding the introduction of teaching on sex and family planning, outlined in your leading article (29 June, p. 686), is as true for those subjects as it is for many other important aspects of medicine which are still outside the normal medical curriculum.

The problems, though, are not just lack of space in the curriculum and resistance by departments but also a complete lack of communication, not only between the departments themselves but also between them and the students they purport to teach. A telling example of this was in my own medical school, where the department of community medicine gave a lecture on the population crisis followed no less than three months later by a lecture from the department of obstetrics and gynaecology on the subject of contraception, to all intents and purposes a completely separate entity.

The introduction of a multidisciplinary course in contraceptive methods, sex counselling, demography, and population dynamics should not just be an excuse for more lectures. It is hardly surprising that medical students faced with slide after slide of

statistical evidence find more stimulation in a cup of coffee. More use must be made of teaching aids, films, and discussion groups related to clinical situations before students should be expected to take an active interest.

In fact, an extracurricular course on "Understanding Sex" was organized by students at Guy's consisting of lectures, discussion groups, and a film. It was well attended and appreciated by the students, which perhaps indicates that medical students, contrary to the picture of an un-receptive group needing to be cajoled into attendance, feel that sex education does occupy an important place in their course that is not yet filled.—I am, etc.,

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Jaundice after Halothane

SIR,—We wish to comment on the letters from Dr. W. H. W. Inman and Professor W. W. Mushin (27 April, p. 220) and Dr. D. Mansel-Jones (p. 221).

In their report (5 January, p. 5) Dr. Inman and Professor Mushin note that "no technique is available which will with certainty distinguish viral hepatitis from post-anaesthetic jaundice," while in their letters they state that "sufficient information to exclude other causes of jaundice was obtained for 111 (85%) of the patients." We are unable to reconcile these apparently contradictory statements. The three points made by Dr. Mansel-Jones in the fourth section of his letter apply to adverse reactions in general, but they should not apply to this specific one.

We are concerned that Dr. Inman and Professor Mushin note in their report that the more rapid onset of jaundice after multiple exposures to halothane provides "strong evidence of a cause-effect relationship between the use of halothane and jaundice." As the ability to differentiate halothane hepatitis from viral hepatitis was essential in the generation of their data, this conclusion is to some extent the result of circular reasoning. It is essential to remember that Klatskin¹ and Trey *et al.*² stressed the importance of multiple exposures to halothane in 1967 and 1968 respectively. Klatskin's uncontrolled data also suggested that there might be a shorter latent period to the onset of jaundice after multiple exposures to halothane compared with that after single exposures to the drug. It is interesting to observe from table II in Dr. Inman's and Professor Mushin's report that the percentage of cases in which the patient suffered multiple exposures to halothane rose in 1969 (1964-1968=78%, 1969-1972=90%, χ^2 test $P < 0.01$). In view of this it would be important to know if the picture relating to the rapidity of onset of jaundice also changed in 1969.

Dr. Inman and Professor Mushin have compared the risk of death in any one year after multiple exposures to halothane with the risk of "death in any one year from infectious hepatitis and acute or subacute hepatic necrosis in the general population." It would have been more appropriate—if indeed it is appropriate to compare numerical data derived from cases submitted voluntarily with anything—to compare the former with the risk of death in the same

year after multiple exposures to non-halothane anaesthetics.

The Mann-Whitney U test seems satisfactory, but while acknowledging that the result would remain "statistically significant" would it not have been more appropriate to use the two-tailed test? We would also like to ask Dr. Inman and Professor Mushin why they assumed that the multiple exposures to halothane rather than another variable, such as the medical condition requiring the additional surgery or the exposure to multiple operations, was the cause of the statistically significant difference. The population exposed to single administrations of halothane also differed from that formed by pooling the patients exposed to two and three administrations of the drug with regard to sex distribution (χ^2 test $P < 0.01$). Perhaps the populations differed in several other respects as well.—We are, etc.,

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- ¹ Klatskin, G., in *Toxicity of Anesthetics*, ed. B. R. Fink p. 159. Baltimore, Williams and Wilkins, 1968.
² Trey, C., *et al.*, *New England Journal of Medicine*, 1968, **279**, 798.

Infections in Asplenic Adults

SIR,—It is of interest that one of the adults with *Haemophilus influenzae* meningitis described by Dr. Susannah J. Eykyn and her colleagues (1 June, p. 463) had previously undergone splenectomy. The authors indicate that splenectomy has been mentioned as a predisposing condition, and I would like to emphasize certain points about the risk of life-threatening infection in asplenic adults which have a bearing on management.

As in children, asplenic adults have a peculiar susceptibility to fulminant pneumococcal infection presenting as meningitis or the Waterhouse-Friderichsen syndrome,¹ with a mortality of 60% in the 40 cases reported in the literature.² In recent reports of serious infection following splenectomy for staging of Hodgekin's disease *H. influenzae* infection has also been prominent, though less frequent than *Streptococcus pneumoniae*, and these two organisms account for the large majority of reported cases of serious sepsis in asplenic patients. The risk is said to be maximal in the first 2-3 years after splenectomy,^{3,4} but this is based on paediatric experience, which is biased by short follow-up after splenectomy.⁵ Excluding those who were followed up for only 2-3 years after splenectomy, eight of 20 cases of serious pneumococcal infection in asplenic adults occurred more than five years after splenectomy.² Fourteen (70%) occurred later than two years after splenectomy, suggesting that penicillin prophylaxis for two years⁶ is unlikely to solve the problem.

These devastating infections are an uncommon complication of the asplenic state, and it seems that the practical approach to management is prompt and effective treatment when they arise. It has been suggested that increased awareness of the risk may have contributed to the lower mortality in

recent reports.² It is recommended that potentially lethal infection with *Str. pneumoniae* or *H. influenzae* be seriously considered in any asplenic patient with pyrexia which is not readily explained and, if leucocytosis is found, that treatment with ampicillin be commenced immediately after obtaining blood for culture. Asplenic patients presenting with meningitis or Waterhouse-Friderichsen syndrome should be treated with a regimen including an antibiotic effective against both *Str. pneumoniae* and *H. influenzae*—for example, intravenous ampicillin—until the causal organism has been clearly identified.—I am, etc.,

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- ¹ Whitaker, A. N., *Medical Journal of Australia*, 1969, 1, 1213.
- ² Ramsay, L. E., and Bouskill, K. C., *Journal of the Royal Naval Medical Service*, 1973, 59, 102.
- ³ *Annals of Internal Medicine*, 1972, 77, 143.
- ⁴ Smith, H., *Medical Annual*, 1973, 91, 278.
- ⁵ Horan, M., and Colebatch, J. H., *Archives of Disease in Childhood*, 1962, 37, 398.
- ⁶ Ravry, M., et al., *Annals of Internal Medicine*, 1972, 77, 11.

Treatment of Genital Herpes

SIR,—Your leading article (1 June, p. 461) describes the local treatment of genital herpes by incorporating a light-sensitive compound into the virus and then irradiating the infected cells. It also underlines the difficulties of evaluating the results of any form of treatment, especially as one of the most important parameters is the subjective index of relief of pain and tenderness in the herpetic lesions. It might have pointed out more emphatically the need to restrict evaluation to the results obtained in cases of primary herpes simplex virus (H.S.V.) infection, as recurrent attacks are usually mild and short-lived.

In genital herpes local applications may be impracticable; the urethra is not uncommonly involved in men and a severe necrotizing cervicitis is present in at least one-third of women with primary vulval herpes. Furthermore, in a smaller percentage of patients there are severe constitutional symptoms, presumably arising from viraemia. A systemic remedy should therefore be our therapeutic goal. Both idoxuridine and cytarabine cause marrow suppression when given systemically and their use would be justified only for life-threatening H.S.V. encephalitis. For the past four years we have used co-trimoxazole in severe cases of primary genital herpes with such good results that we are undertaking a double-blind trial to provide a firm evaluation of this simple, safe, and inexpensive form of treatment.—We are, etc.,

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Beta-blockade in the Presence of Renal Disease and Hypertension

SIR,—We were most interested in the results of investigations by Drs. F. D. Thompson and A. M. Joekes (8 June, p. 555). They support the widely held impression that beta-blockers do not adversely affect renal

function in most hypertensive patients. The results do not, however, provide evidence to refute our suggestion that beta-blockers may cause deterioration in renal function in some patients with chronic renal failure (27 April, p. 193). It is significant that three consecutive patients in whom there was an association between deterioration in renal function and the introduction of beta-blockers were admitted to a specialist renal unit in the space of six months. Having excluded other likely causes of deterioration in renal function we could only conclude that beta-blockade might be responsible. Recent evidence¹ that the incidence of atherosclerotic heart disease in patients with renal failure is high supports our view that there may be some patients with chronic renal failure who are particularly susceptible to the negative inotropic and chronotropic effects of beta-blockade on the heart.

We await with interest the full results of the work of Drs. Thompson and Joekes and in particular a detailed analysis of the effects of beta-blockade on renal function in those patients whose creatinine clearance is less than 30 ml/min.—We are, etc.,

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Department of Medicine,
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- ¹ Lindner, A., et al., *New England Journal of Medicine*, 1974, 290, 697.

Puerperal Rubella Vaccination and Anti-D Immunoglobulin

SIR,—We were interested to read the letter from Mr. B. Alderman and Mr. D. W. Charters (29 June, p. 724).

It has been the practice in Bradford to perform rubella haemagglutination inhibition (H.I.) tests routinely in pregnancy at the first antenatal attendance and to offer rubella immunization with Almevax vaccine in the puerperium to women with titres of 1/16 or less. Some of these patients to whom rubella immunization was offered had been given anti-D immunoglobulin, and in view of suggestions that this might prevent a successful vaccination we have followed up as many patients as possible to see if they had a serological response to the rubella vaccine.

The number of results so far available is very small. Of four women whose antenatal H.I. titres were less than 1/8 the post-vaccination titres were 1/128 in two cases, 1/64 in one, and 1/32 in one. In three of the four cases two additional H.I. tests were done after delivery, before rubella immunization was performed—namely, before and after the administration of anti-D immunoglobulin; all these titres also were less than 1/8. The postvaccination specimens were collected 51–60 days after immunization. Seven women whose prevaccination H.I. titres were 1/8 or 1/16 and who also received anti-D immunoglobulin showed less response and had postvaccination titres which were only 2- or 4-fold higher or remained unchanged.

Though we do not have enough data to permit firm conclusions, it does seem that at least those patients who have no detectable rubella antibodies are likely to develop a satisfactory serological response following rubella vaccination in spite of the prior

administration of anti-D immunoglobulin. An extended investigation to confirm our preliminary findings would be desirable, and we should be interested to know the experience of other workers in this field.

We wish to thank the consultant obstetricians in Bradford for their co-operation in this investigation and Dr. R. J. Rand and Dr. Brij B. Khurana for their assistance.

—We are, etc.,

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Healing of Leg Ulcers

SIR,—My attention has been drawn to an erroneous reference in my paper "Vertical Leg Drainage of Oedema in Treatment of Leg Ulcers" (15 June, p. 581). The correct reference is Myers, H. B., and Cherry, G. (1971), *American Surgeon*, 37, 167.

It is possible that my paper conveyed the impression that I considered my healing rates equalled those quoted by Myers and Cherry. This was not my intention; their healing rates were much faster, but their ulcers were much bigger than most of mine, and in the similarly large ulcers in my series the rate was much above my average.

It is worth emphasizing that my method is cheaper, especially in the absence of loss of work time for the patient.—I am, etc.,

I. H. J. BOURNE

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HI Antibodies to Influenza A/Finland/1/74

SIR,—During the epidemic season of 1973–4 influenza outbreaks in Finland were caused mainly by B "intermediate" strains, but small outbreaks and scattered cases due to influenza A also occurred throughout the country. From a follow-up study the rate of influenza A infections among adults was clearly below 10%. The 28 influenza A isolates from 21 patients were found to be antigenically closer to A/Port Chalmers/1/73 than to the previous variants of Hong Kong virus. The strains studied in the World Influenza Centre differed even from the Port Chalmers strain by showing very low, if any, HI titres with anti-A/Hong Kong/1/68 serum. Similar strains were isolated in the Democratic Republic of Germany, Federal Republic of Germany,¹ and Norway.²

During the recent influenza epidemics an HI titre of ≥ 40 has appeared to confer protection against infection.³ In pre-epidemic sera collected in Finland in autumn 1973 from 40 conscripts and from 65 pregnant women the percentages of cases with an HI titre of ≥ 48 to A/Finland/1/74 were 30 and 27. The corresponding percentages of cases with HI antibodies to A/Hong Kong/8/68 were 65 and 75. In a series of 43 acute phase sera from A/Finland/74 patients the highest titre of the homologous antibodies was 24.

We have analysed the HI antibody responses of influenza A patients during the five H3N2 epidemics occurring in Finland. All patients were conscripts of 18–21 years. The acute sera had been taken not later than in the fourth day from the onset of illness,