patient stay required, and any step that can make it safer is worth while.—I am, etc.,

MICHAEL BRUDENELL

King's College Hospital,
London S.E.5

SIR,—I note that in the three cases of accidental insufflation of gas into the uterine cavity reported by Drs. M. B. Barnett and D.T.Y. Liu (23 February, p. 328) "the pressure was continuously monitored and never allowed to exceed 30 mm Hg." This level would seem to me to be excessive.

Many of the hazards of laparoscopy are associated with induction of the pneumoperitoneum. These can involve injecting gas into many areas such as bowel, subperitoneal tissues, the uterus itself, and other tissues, and it is my experience that in all such cases the readings of induction pressure were higher than normal, which I take to be between 10 and 12 mm Hg. In fact if the reading is higher than 14 mm Hg I always remove the Verres's needle and reinsert it. It is a common finding that the fundus of the uterus has a small nick in it, particularly when sterilization is carried out after termination at more than 12 weeks' pregnancy.

I would suggest that if such dangers are to be avoided pressures should be continuously monitored and never allowed to rise above 14–16 mm Hg, the higher level being associated with inspiration, particularly if the patient is on an insufflator.—I am, etc.,

I. K. MATHIE

Department of Obstetrics,
North Tees General Hospital,
Stockton-on-Tees

Influenza Virus Vaccination and Renal Transplant Rejection

SIR,—Briggs *et al.*¹ have drawn attention to an apparent association in their patients between a severe attack of influenza and acute rejection of a renal transplant. They suggested that infection with influenza virus may have caused a general stimulation of the immune response of the patients. They questioned the advisability of immunizing patients with transplants because influenza vaccine may produce a general stimulation of the immune response. Commercial inactivated influenza virus vaccines contain variable amounts of chick embryo antigens which may be similar to or cross-react with human tissue antigens. These vaccines may, for example, stimulate a significant rise of anti-A isoagglutinins in healthy people of blood groups O or B.^{2,3}

It has been the routine policy of this unit to offer influenza virus vaccination to patients who are awaiting renal transplantation and also to those who have received a transplant. After the report by Briggs *et al.* we have carefully followed up the patients with transplants who received influenza virus vaccine during the autumn of 1972. One patient had a rejection episode which occurred six weeks after vaccination. However, this occurred after a New Year week-end in Scotland when the patient omitted to take his immunosuppressive drugs, which we feel is more likely to have caused the rejection episode than the vaccination. The remaining 17 patients did not have any

episode of rejection over a three-month period after the vaccination. One patient who did not receive vaccine developed a moderately severe attack of influenza but this was not followed by a rejection episode.

During the autumn and winter of 1973 22 patients who had received renal transplants and four normal subjects acting as controls were investigated for the presence of cytotoxic antibodies in the serum before and after administration of inactivated influenza virus vaccine B.P. by intramuscular or subcutaneous injection. The post-immunization blood samples were taken from the controls after 10–14 days and from the transplant recipients at their next visit, usually 14–21 days after immunization. Serum was separated at once and was stored at -20°C until tested. All the samples were tested for HL-A antibodies using a two-stage microcytotoxicity technique.⁴ Lymphocyte suspensions were prepared from freshly drawn blood by flotation,⁵ and the panel of cells used contained the following antigens: HL-A 1, 2, 3, 9, 10, 11, W 28, W 29, W 32, HL-A 5, 7, 8, 12, 13, W 5, W 10, W 14, W 15, W 16, W 17, W 18, W 22, W 27. The results are shown in the table.

Subjects	Presence of Cytotoxic Antibodies	
	Before Immunization	After Immunization
3 controls	—	—
1 control	+	+†
18 patients	—	—
3 patients*	+	—
1 patient*	—	+

*Prevaccination specimen taken three weeks after transplantation and several months before vaccination.
†Specificity and titre unchanged from earlier observation.

In only one of the 22 patients was antibody detected which had not been present before vaccination. In this patient (blood group A) the first sample was taken three weeks after transplantation and the vaccination was carried out 13 months later without an immediate prevaccination specimen being obtained. It is therefore uncertain whether the presence of cytotoxic antibody after vaccination was related to this measure. None of the patients vaccinated, including the one with cytotoxic antibodies, showed any evidence of rejection during the period after vaccination.

This evidence does not support the concept that influenza virus vaccination is likely to provoke a rejection episode in a patient who has had a kidney transplant. The evidence that it may be responsible for the appearance of cytotoxic antibodies rests on one patient, in whom their appearance may well have been a response to the presence of the kidney graft itself.—We are etc.,

J. CONNOLLY
J. DOUGLAS
R. KUMAR
D. MIDDLETON
J. MCEVOY
S. NELSON
M. G. MCGEOWN

Renal Unit,
Belfast City Hospital,
Belfast

¹ Briggs, J. D., Timbury, M. C., Paton, A. M., and Bell, P. R. F., *British Medical Journal*, 1972, 4, 520.
² Springer, G. F., and Tritel, H., *Science*, 1962, 138, 687.

³ Forsyth, J. R. L., and Wilson, T. E., *Journal of Hygiene*, 1968, 66, 1.

⁴ Sanderson, A. R., *Nature*, 1967, 215, 23.

⁵ Harris, R., and Ukacjiofo, E. O., *British Journal of Haematology*, 1970, 18, 229.

Reactions to Immunization

SIR,—With reference to Dr. E. P. James's letter (16 February, p. 287), studies of the immunological system in the neonate are complex. Premature infants are very likely to develop hypogammaglobulinaemia.¹ Furthermore, up to 4% of babies born at full term are slow to replace maternal IgG and 25% of these (1% of all births) will suffer a transient but often severe hypogammaglobulinaemia.² There are in addition those infants who suffer from a primary immune deficiency such as Bruton's hypogammaglobulinaemia. Vaccination with an attenuated live vaccine is an extremely hazardous and frequently fatal procedure in all such infants. Accordingly it is essential that a careful check be made both of the infant to be vaccinated and of the family, particularly siblings, for a history of abnormally frequent or severe infections. Then if necessary the immunoglobulin levels should be measured before vaccination—it is obviously not practicable to do this before vaccination in every infant.

Adherence in this practice will certainly contribute to a reduction in the incidence of complications following vaccination and ensure that the technique of active immunization retains its place as a valuable prophylactic procedure.—I am, etc.,

RALPH H. ROUSSELL

Hoechst Pharmaceuticals,
Hounslow, Middlesex

¹ Hobbs, J. R., and Davis, J. A., *Lancet*, 1967, 1, 757.

² Hobbs, J. R., *Proceedings of the Royal Society of Medicine*, 1968, 61, 883.

Jaundice after Halothane

SIR,—We should like to comment on the report by Dr. W. H. W. Inman and Professor W. W. Mushin based on reports of jaundice attributed to halothane received by the Committee on Safety of Medicines (5 January, p. 5).

We believe that a report of this nature and potential international importance deserves a more detailed explanation of the method by which the committee collects its cases than that provided by the first three lines of the section entitled "Material and Methods." Who is asked to submit cases? How much information is requested? To what extent does the committee verify the information it receives? To what extent does the committee seek additional pertinent information relating to specific cases? Our final question concerning this aspect of the report is, however, the most important. What specific diagnostic criteria does the committee insist upon before a case report is classified as "attributing" a particular drug reaction to a specific medicine? As halothane hepatitis is indistinguishable from viral hepatitis, a point acknowledged by Dr. Inman and Professor Mushin, this question is of extreme importance to those who are interested in evaluating their report. The fact that the authors make a point of noting that "in the nine-year period . . . no report attributed jaundice to