tral Public Health Laboratory, Colindale Avenue, London N.W.9 5HT phone 01-205-7041.

In Scotland similar immunoglobulin is prepared at the Protein Fractionation Centre and can be obtained by contacting the director of the appropriate regional blood transfusion centre who will also provide information regarding the local follow-up arrangements for the recipient.—I am, etc.,

D. N. S. KERR

on behalf of the Medical Research Council Working Party on Specific Immunoglobulin for Serum Hepatitis

Department of Medicine,
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1 Cossart, Y. E., *Proceedings of the European Dialysis and Transplant Association* 1972, 9, 235.

2 Krugman, S., Giles, I. P., and Hammond, J., *Journal of the American Medical Association* 1971, 218, 1665.

3 Soulier, J.-P., Couroucé-Pauty, A.-M., and Benamon-Djiane, D., *Revue Française de Transfusion*, 1972, 15, 377.

Hazards of Laparoscopy

SIR,—I should like to refer to the mode of introduction of the pneumoperitoneum needle. It is this part of the operation which registrars find most difficult and why we suggested (30 June, p. 773) a different site for insertion in the *unexceptional* case. I have the greatest admiration and respect for Mr. Patrick Steptoe (11 August, p. 347) but respectfully suggest that a technique which is easier to learn is likely to be safer as far as surgical trainees are concerned. In Winchester we have found that registrars find it easier to learn the technique of inserting the needle about half-way between the symphysis pubis and the umbilicus. The operator's left hand tenses the abdominal skin while palpating the sacral promontory. The needle "plunges" into the hollow of the pelvis with a distinctive feel. It is, of course, essential that the patient is in the Trendelenburg position and that an assistant holds the Spackman's cannula in such a way as to anteverte the uterus as far as possible. This method is contraindicated in patients with a pelvic tumour, when a technique such as described by Mr. Steptoe is preferred.

This method is quite different from the standard technique because the abdominal wall is not lifted away from the posterior abdominal wall and relies for its safety in directing the needle into the pelvic cavity. We find it useful to keep the pneumoperitoneum needle in situ; it can be used to display the pelvic viscera or aspirate cysts and often avoids the need to insert another trocar and cannula. Since adopting this technique (which is not unique to Winchester) we have had no laparoscopy failures. The uterus has been punctured three times in about 200 operations but with no sequelae.

Trainees need to be taught the several means of introducing the pneumoperitoneum needle and, like Keijland's forceps, this means tuition by the expert.—I am, etc.,

A. D. NOBLE

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Winchester

Depression and Organic Disorder

SIR,—I would agree with Dr. W. Sircus (1 September, p. 480) that it is important to

consider a lurking neoplasm or indeed any lurking organic disorder as an aetiological factor in a depressive illness occurring for the first time in a man over 70 years of age. However, he is over-stating his case when he suggests that the depression in the case presented should have alerted the clinicians, there being at least three other possible causes of a depressive illness in this instance.

Firstly, the patient was reported as being ostensibly depressed following the sudden accidental death of his grandson six months before. A prolonged bereavement reaction cannot be ruled out. Secondly, he was noted to be depressed four years after his first consultation. During this time he had been receiving that well-known depressant of both blood pressure and mood alpha-methyl dopa. Thirdly, over the following months the patient had almost continuous abdominal pain unrelieved by medical treatment. He had numerous and repeated investigations, including biopsies and endoscopies. At one point after almost dying from a haematemesis and developing a urinary tract infection he went into urinary retention as a result of his antidepressant medication. Thereafter he had chest pain, dyspnoea, haematemesis, and haemoptysis. It is then said that "during the next 10 days depression was the most striking feature." Might I venture to suggest that any other mood would have been highly unusual considering what he had endured?

Finally, while Dr. Sircus and I agree on the importance of being suspicious of such a depression I note that in Mr. A. N. Smith's table of 11 symptoms occurring in carcinoma of pancreas nowhere is there any mention of depression.—I am, etc.,

GEORGE DODDS

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Aberdeen

Protection of Cytomegalovirus-infected Cells by IgG Antibody

SIR,—You recently published a letter (12 May, p. 364) from this laboratory recording the immunological destruction in vitro of cytomegalovirus (C.M.V.)-infected cells. We have recently repeated these experiments with the same ground squirrel cell cultures infected with C.M.V. and by means of the same laboratory techniques, but using in addition pooled ground squirrel sera reactive in the complement fixation test and also its IgG fraction separated by rivanol (ethacridine) treatment¹ and checked by immunodiffusion tests performed with anti-ground-squirrel-protein serum produced in rabbits. The results revealed that antibodies of the IgG class do not lyse C.M.V. inclusion cells in the presence of fresh guinea-pig serum referred to as complement (C'). Moreover, when monolayers treated with 20% IgG were washed and exposed to positive serum in the presence of complement, lysis of C.M.V.-infected cells required an incubation time 2-6 hours longer than in control cultures not treated with IgG. Control tests were also performed omitting either the antibody or the complement.

Our findings indicate that the major portion of antibody activity against C.M.V. inclusion cells lies in the IgM fraction. On the other hand, the delay of cell lysis caused

by IgG antibodies suggests that the antigenic sites on the cell surface are far apart and that bridging of attached IgG molecules is not possible. Hence there is no lysis, but IgG molecules are temporarily blocking all the antigenic determinants. Such blocking effect of IgG molecules has also been observed in the course of C.M.V. immunofluorescence tests.² Thus an imbalance of the relative amounts of different classes of immunoglobulins may protect C.M.V. inclusion cells against the lytic action of IgM antibody.

These results obtained with the ground squirrel C.M.V. model are not necessarily pertinent with respect to human C.M.V. disease. Two facts should be remembered, however. First, the human newborn receives IgG from his mother as almost the exclusive immunoglobulin, and it fails to confer on him effective protection³ against the appearance of C.M.V. inclusion cells in various tissues and organs and the associated severe clinical symptoms emerging during congenital disease. Secondly, commercial gammaglobulin preparations which provide only IgG in appreciable amounts and practically no IgM,² were widely used during the 1950s and proved therapeutically ineffective.⁴—We are, etc.,

PETER DIOSI
GEORGETA HERZOG

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1 Horejsi, J., and Smetana, R., *Acta Medica Scandinavica*, 1956, 155, 65.

2 Schmitz, H., and Haas, R., *Archiv für Gesamte Virusforschung*, 1972, 37, 131.

3 Weller, T. H., *Journal of Infectious Diseases*, 1970, 122, 532.

4 Hanshaw, J. B., *Journal of Infectious Diseases*, 1971, 123, 555.

Endotoxic Shock Complicating Transhepatic Cholangiography

SIR,—I read the article by Mr. M. R. B. Keighley and others (21 July, p. 147) with considerable interest though I could not but wonder what the indication was for the extensive investigations recorded, the last of which unfortunately resulted in the patient's death, when it would appear from reading the article that a simple laparotomy would have established the diagnosis and facilitated the immediate treatment.—I am, etc.,

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Antibiotic-induced Meningitis

SIR,—The leading article "Antibiotic-induced Meningitis" (18 August, p. 336) creates mysteries where none exist. The initial misconception is in the first paragraph where it is stated that "it is a novel idea that a fresh infection arising during treatment should be caused by a sensitive organism and should involve the meninges." Review of the eight cases cited,¹⁻⁴ shows that adequate information is available for six. In each of these there is ample evidence to support the view that meningitis was an extension of a primary infection situated outside the central nervous system. In each there was conclusive evidence of blood-borne infection. In each the meningeal infection was apparently caused by the same organism

and was a consequence of the bacteraemia and, hence, of the primary infection. The fact that meningitis, once established, did not respond to therapy with cephalothin is a reflection of the low and erratic penetration of the antibiotic into the cerebrospinal fluid. There is absolutely no evidence to suggest that the meningeal infection was truly a "fresh infection" or, indeed, that it was "antibiotic induced."

The second misconception also occurs in the first paragraph. The comment is made that "apparently cephalothin is the only antibiotic against which this accusation can be levelled." This view is not shared by Mangi *et al.*,¹ who state that "meningitis is a possible complication when septicaemia is treated with any antibiotic that does not easily pass the blood brain barrier. A high degree of suspicion of meningitis is warranted for any patient with bacteraemia who does not respond to cephalothin or any other antibiotic with moderate cerebrospinal fluid penetration." Even a superficial review of the literature shows that meningitis developing during appropriate antimicrobial therapy has been reported for other antibiotics—for example, tetracycline,² penicillin,³ lincomycin,⁴ colistin.⁵ In fact, a series of 60 children had received such antibiotics as penicillin, tetracycline, ampicillin, erythromycin, and sulphonamide for respiratory tract infections, etc., prior to the development of meningitis.⁶ There is, therefore, nothing unusual or unique to cephalothin in this complication. Furthermore, the leader writer chose to ignore Mangi and colleagues' comments regarding such contributing factors as trauma due to lumbar puncture as a mechanism introducing bacteria into the spinal fluid in three patients; debilitating disease with probable diminishing host resistance in four; and rather low cephalothin dosage in two.

The conclusion in the leading article—namely, "what is in question here is not the treatment of meningitis but that of infections located elsewhere which may apparently be followed by meningitis if cephalothin is used in their treatment," requires clarification. Since cephalothin was introduced many millions of patients have been treated with it in many countries of the world. During that time the concomitant occurrence of meningitis has been mentioned in four reports involving a total of eight patients. It would be quite illogical to restrict the use of cephalothin for this reason.

Finally, the article refers to two reports^{10 11} from Paris and Rouen respectively, in each of which three patients are described who developed renal failure during treatment with cephalothin and gentamicin. As gentamicin is known to have nephrotoxic potential¹² it is difficult to determine what role, if any, cephalothin played in this matter.—I am, etc.,

W. I. H. SHEDDEN

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¹ Mangi, R. J., Kundargi, R. S., Quintiliani, R., and Andriole, V. T., *Annals of Internal Medicine*, 1973, 78, 347.

² Turck, M., Anderson, K. N., Smith, R. H., Wallace, J. F., and Petersdorf, R. G., *Annals of Internal Medicine*, 1965, 63, 199.

³ Almond, H. R., *New England Journal of Medicine*, 1969, 281, 218.

⁴ Lerner, P. I., *American Journal of Medical Sciences*, 1969, 257, 125.

⁵ Apicella, M. A., Perkins, R. L., and Saslaw, S., *American Journal of Medical Sciences*, 1966, 251, 266.

⁶ Torphy, D. E., and Ray, C. G., *American Journal of Diseases of Children*, 1970, 119, 336.

⁷ Hansman, D., and Gibbs, M., *New England Journal of Medicine*, 1972, 287, 201.

⁸ Price, D. J. E., and Sleight, J. D., *Lancet*, 1970, 2, 1213.

⁹ Jarvis, C. W., and Saxena, K. M., *Clinica Pediatrica*, 1972, 11, 201.

¹⁰ Kleinknecht, D., Ganeval, D., and Droz, D., *Lancet*, 1973, 1, 1129.

¹¹ Fillastre, J. P., *et al.*, *British Medical Journal*, 1973, 2, 396.

¹² Kahn, T., and Stein, R. M., *Lancet*, 1972, 1, 498.

* * Few readers are likely to accuse us of the first of these "misconceptions." We wrote that four of these five patients had positive blood cultures, and that the same organism caused the subsequent meningitis. This infection was clearly "fresh" only in the sense of its new location. As regards the second, there are naturally many instances in which meningitis has developed during treatment with other antibiotics, but if the cases described by Mangi and his colleagues were not at least unusual, if not indeed unique, why should they have been considered worthy of publication in a leading American journal? Their essential feature is the very short interval lapsing between the start of treatment and the onset of meningitis.—Ed., *B.M.J.*

Hypomagnesaemia after Parathyroidectomy

SIR,—Having had a similar experience to that described by Dr. C. T. A. Jones and others (18 August, p. 391) we wish to confirm their suggestion that hypomagnesaemia should be regarded as an important development after parathyroidectomy in patients with bone disease in hyperparathyroidism.

Our patient, a man aged 35, presented early this year with pathological fractures. Radiologically there were characteristic changes of hyperparathyroidism and gross demineralization. Serum calcium concentration was 7.3 mEq/l., with total protein 6.9 g/100 ml, plasma phosphate 0.9 mg/100 ml, serum magnesium 1.4 mEq/l., and serum alkaline phosphatase 414 IU/l. Serum parathyroid hormone concentration was 13.8 ng/ml. A carcinoma of the left upper parathyroid gland was excised (Mr. C. W. A. Falconer).

As a rapid fall in serum calcium was anticipated, a single dose of 15 mg of calciferol was given intravenously immediately after the operation and calcium gluconate was infused intravenously in an amount equivalent to 20 g of elemental calcium in five days. Mild symptoms of paraesthesiae in the extremities and around the mouth appeared when oral calcium (Sandocal) was substituted. These symptoms became more severe, with a positive Chvostek's sign and occasional spontaneous facial twitching, despite increasing the oral calcium intake to the equivalent of 12 g of elemental calcium daily along with 2.5 mg daily of oral calciferol. On the 20th day he developed dysarthria and weakness of the right lower face when the serum calcium level had fallen to 2.5 mEq/l., with serum magnesium 1.15 mEq/l. Intravenous calcium gluconate (20 ml of 10% solution) raised the serum calcium to 3.3 mEq/l. but had little effect on the symptoms. The dysarthria and facial weakness disappeared immediately after the intravenous injection over two minutes of 500 mg of magnesium chloride. Intravenous infusion of magnesium chloride

and calcium gluconate was maintained for 48 hours and then oral magnesium (Sandoz Ltd.) and calcium (Sandocal) were given. Despite the subsequent fall of serum calcium concentration to a level at which a positive Chvostek's sign with moderate paraesthesiae had previously occurred, these features did not return, possibly because the serum magnesium was now normal.

We would therefore support the contention implied by Dr. Jones and his colleagues that it is important to monitor the serum magnesium concentration after parathyroidectomy for hyperparathyroidism in patients with bone disease. We hope to publish a more complete account, including balance data, in the future.

We wish to thank Dr. J. L. H. O'Riordan for the parathyroid hormone assay.

—We are, etc.,

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J. A. STRONG

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Incidence and Prevalence

SIR,—It is apparent that the author of your leading article "Screening for Glaucoma" (8 September, p. 511) has regrettably failed to realize that the terms "incidence" and "prevalence" are not synonymous.

Prevalence covers all cases detected at a designated time in a certain population, whereas incidence implies new cases occurring during a defined period of time in a certain population. Thus the 55 cases detected from examining a population of 5,941 on a single occasion (a cross sectional or point prevalence study) represents a prevalence (not incidence) of 0.93%.

However, the five new cases detected from following up 212 persons over five to seven years (a prospective, follow-up, or longitudinal study) represents an incident of 2.63% (presumably allowing for patients lost to follow-up).—I am, etc.,

ROSS ULMAN

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Impatient Patients

SIR,—One appreciates Dr. J. Mahmood's (8 September, p. 546) over-sensitivity and possible frustration at the mini-epidemic of patients requesting referrals for investigation before asking his advice on diagnosis and treatment. Granting these desires and then having the patient removed from his list is certainly one possible remedy, as Dr. Mahmood suggests. Another possible approach is to put the patient at ease by agreeing to all the demands for investigations, or pills and opinions, and then gently coax out the reasons for these requests. This can be quite revealing and rewarding to both doctor and patient, and usually dispenses with the need for any tests, potions, or opinions. (Description before prescription.) Should however the patient be correct in his guess he can be complimented and appropriate tests, or therapies, instituted.

Though this approach takes longer initially, the doctor fulfils his role as teacher