SIR,—While the report by Dr. D. P. Davies and others (1 September, p. 476) shows a clear association between an increased incidence of neonatal jaundice and induced labour there can be little to commend the title of their communication. They discuss in some detail the mechanism by which hepatic enzyme immaturity might occur in the offspring of women who do not spontaneously enter labour. They quote the "gestational age" as being around 39 weeks in the group of women whose labour was induced without reference to the well recognized inaccuracy of calculating the anticipated date of confinement from a patient's recollection of her last period.

There is a strange uniformity of the 39-week figure in the three groups. I submit that those who started spontaneously in labour might well have been at term, and those who were induced (presumably because they failed to start in labour at "39 weeks") might have been significantly immature. It is seldom that the precise date of conception can be ascertained and, though postmaturity is well recognized, the majority of induced labours will probably be preterm.

The title of the article could only be justified if the authors had compared their results with a control series in which labour was induced without oxytocin. It should surely have read "Neonatal Jaundice and Induced Labour."—I am, etc.,

WILFRID G. MILLS

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SIR,—Dr. D. P. Davies and others (1 September, p. 476) wonder if the infants in Group C (oxytocin induced) are particularly susceptible to hyperbilirubinaemia. Could not the explanation be that a fair proportion of these babies are immature?

Estimation of the gestational period is nowadays notoriously difficult. Could not this immaturity be the reason why the mothers had not gone spontaneously into labour?—I am, etc.,

M. C. R. FISHER

Oxford

Apnoea after Sacral Extradural Analgesia

SIR,—Dr. S. V. Humphries's interesting "Personal View" (25 August, p. 452) points out a danger of sacral extradural analgesia and how he dealt with it successfully. This is an excellent and safe form of pain relief increasingly being used in both our labour wards and operating theatres.

The risk of puncture of the spinal dural sac, a structure which usually but not always ends at the level of the second sacral vertebra, can be minimized by using a needle no more than 4 cm and by inserting it no further once the sacrococcygeal membrane has been pierced. In spite of care and considerable experience in the use of the technique, I have pierced the dura in this situation twice in one morning. The injection of the local analgesic solution should not be made until the anaesthetist is certain that neither blood nor cerebrospinal fluid can be aspirated. Should cerebrospinal fluid appear, while experienced workers may decide to carry on with the form of analgesia, the occasional anaesthetist would be well advised to abandon it to avoid the possibility

of apnoea, so dramatically described by Dr. Humphries.

I am writing this letter to defend an excellent and safe form of pain relief, which, however, may like other techniques result in avoidable complications. It is extremely rare for harm to come to patients who develop apnoea after extradural block, either lumbar or sacral, if they are adequately treated by intermittent positive pressure ventilation, plasma volume expanders, elevation of the legs, and very occasionally the injection of pressor amines.—I am, etc.,

J. ALFRED LEE

Southend General Hospital

Delayed Attacks of Malaria in Visitors to the Tropics

SIR,—I feel sure that Dr. Paul Horstmann (25 August, p. 440) would have changed the wording—and perhaps the title—of his article if he had been able to consult some of the papers on this subject published in the early 1950s. The development of a primary attack of vivax malaria 6-14 months after leaving the malarious area was commonplace in servicemen returning from the war in Korea. This long latent period was regarded as typical of temperate zone strains of *Plasmodium vivax* and contrasted with the short latent periods found in a number of tropical zone strains, notably those from New Guinea. From the details given, Dr. Horstmann's patients might have acquired their vivax infections almost anywhere along the route to India.

I live in retirement and can quote only three references,¹⁻³ but more should be available to anyone within reach of a library dealing with tropical medicine. Dr. Horstmann's article may well have served a useful purpose by reminding today's doctors that these long latent periods do occur in some of the vivax malaria infections that might develop in returned travellers.—I am, etc.,

T. WILSON

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¹ Covell, G., *Journal of Tropical Medicine and Hygiene*, 1954, 57, 151.

² Field, J. W., and Shute, P. G., *Studies from the Institute of Medical Research, Malaya*, No. 24, 1956.

³ Hankey, D. D., et al., *American Journal of Tropical Medicine and Hygiene*, 1953, 2, 958.

SIR,—Dr. Paul Horstmann's interesting paper (25 August, p. 440) is a salutary reminder of the well-known fact that chemoprophylaxis with chloroquine must not be mistaken for causal prophylaxis (especially when it comes to *Plasmodium vivax*). The latter results from the action of drugs on the pre-erythrocytic stages of plasmodia and cannot normally be obtained by 4-aminoquinolines. On the other hand, antifolic drugs, such as pyrimethamine or proguanil, have causal, prophylactic action, especially on *P. falciparum*.^{1,2}

Nevertheless, 4-aminoquinolines exert a high degree of suppressive, antiparasmodial effect, which is greater for *P. falciparum* than for *P. vivax*. This explains why persons exposed to malaria and given insufficient dosage of 4-aminoquinolines, during or shortly after their exposure, may have delayed attacks of *P. falciparum* but particularly of *P. vivax* and other relapsing infec-

tions. In Dr. Horstmann's study of six persons who had a delayed attack of vivax malaria the once-weekly dosage of chloroquine (500 mg of chloroquine phosphate, equivalent to 300 mg of base) was manifestly insufficient, especially as the drug regimen was limited to two weeks after the group's return to Denmark. The recommendations adopted by the World Health Organization,^{3,4} and generally accepted, call for at least four weeks of chloroquine prophylaxis at the above dosage after returning to a non-malarious area. Even then many *P. vivax* infections cannot be suppressed and the delayed primary attack or the first clinical relapse may occur several months later.

This drug-induced delay of the primary attack must not be confused with the infection by some *P. vivax* strains having a naturally long incubation period. It is regrettable that in the discussion of Dr. Horstmann's paper this essential difference has not been sufficiently stressed or fully explained. On the other hand, Dr. Horstmann's remarks concerning the practical diagnostic importance of recognizing the possibility of malaria in persons who were exposed to the infection several months before are pertinent and timely.—I am, etc.,

L. J. BRUCE-CHWATT

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London W.C.1

¹ Peters, W., *British Medical Journal*, 1971, 2, 95.

² Bruce-Chwatt, L. J., *British Medical Journal*, 1971, 2, 91.

³ The Ross Institute Information and Advisory Service, Bulletin No. 2, *Antimalarial Drugs*. London, Ross Institute, 1972.

⁴ World Health Organization, *Chemotherapy of Malaria and Resistance to Antimalarials*, Technical Report Series No. 529, Geneva, W.H.O., 1973.

Specific Immunoglobulin for Prevention of Serum Hepatitis

SIR,—A limited supply of immunoglobulin containing a high titre of antibodies to hepatitis B-associated antigen (HB-Ag) has been prepared at the Lister Institute and will be made available through the Medical Research Council for a series of controlled clinical trials.

It has been decided, however, that there is one situation in which the uncontrolled use of this material is justified. There is already considerable evidence for the value of this¹ and similar^{2,3} material in preventing serum hepatitis after inoculation of material containing HB-Ag. Consequently a limited supply has been made available for distribution through the Public Health Laboratory Service for the treatment of patients, staff, and other persons who are accidentally inoculated with infective material such as blood products, and laboratory reagents which are known to contain the antigen. The recipient and the physician administering it will be asked to participate in a follow-up study which is being conducted by the Medical Research Council to establish its effects and to find the incidence of adverse reactions, if any occur.

In the event of a suspected accident involving inoculation with infective material or splashing of such material into the mouth or conjunctival sac, physicians should contact the nearest Hepatitis Reference Laboratory of the Public Health Laboratory Service, or in cases of doubt, should call Dr. Sheila Polakoff or Dr. Yvonne Cossart at the Cen-

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

Ross Clinic,
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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

Timisoara, România

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