after the pregnancy has occurred. The ante hoc promise would have contractual significance, but the practitioner could not know that he would be able to fulfil the contract.—I am, etc.,

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Sensitivity to Rifampicin

SIR,—In the summary of their paper on this subject (25 May, p. 415), Dr. J. C. Pujet and his colleagues draw two main conclusions: firstly, that rifampicin dosage and serum concentration are "predominating factors" in the occurrence of adverse reactions to the drug and, secondly, that if it is considered necessary to continue giving rifampicin to a patient known to be intolerant to the drug, antibody titres during the 24 hours after the administration of a dose "must be measured to find when they are lowest, which determines the 'un-reactive period,' and when a further dose may be safely given." Neither of these conclusions is warranted by the information presented or by other published work.

Their conclusion on serum rifampicin concentration is based on measurements from only three patients with adverse reactions, two of whom had acute episodes (one of haemolysis, the other of anuria) which could have produced a temporary failure to metabolize or excrete the drug. Furthermore, though the authors refer to "hepatic disorder" in 39 patients, they do not state whether these 39 included one or more of the three on whom the serum rifampicin concentrations were measured. This is an unfortunate omission since rifampicin clearance may be considerably impaired during transient abnormalities of liver function.¹ It cannot in any case be assumed that patients who develop adverse reactions to rifampicin do so because of impaired clearance of the drug from the serum until a properly controlled study has provided evidence for such a hypothesis. The impaired clearance could just as well be an effect of intolerance as a cause of it.

We have compared our own data on maximum serum rifampicin concentrations in two groups of patients on once-weekly rifampicin, the first during adverse reactions,¹ the second with no adverse reactions.^{2,3} The geometric mean of the peak serum concentrations for 10 patients during reactions was 38.0 µg/ml, whereas the mean for 12 patients with no reactions was 25.7 µg/ml. Even though this difference is significant ($P = 0.01$) there was no evidence of variation from patient to patient in their serum concentrations among those with no reactions.³ Thus it appears probable that patients who have already become intolerant clear the drug from their serum less rapidly than do those without intolerance and do not develop intolerance because of a preceding tendency to have higher concentrations.

Although rifampicin dosage in intermittent regimens is known to affect the incidence of adverse reactions, a recent controlled trial has shown that the rhythm of administration of the drug is by far the more important factor.⁴⁻⁶ Thus the incidence of reactions in patients given

rifampicin once a week was significantly higher ($P < 0.001$) than that in patients on the same dosage twice weekly, and the incidence during once-weekly chemotherapy was significantly lower ($P = 0.025$) if the intermittent phase was preceded by two months of daily treatment. Adverse reactions of the type discussed by Dr. Pujet and his colleagues did not occur at all during fully supervised daily administration. A moderate reduction in rifampicin dosage stopped adverse reactions in some patients. However, if it failed to do so a change to a daily rhythm of administration almost invariably succeeded. Of 111 patients with reactions to intermittent rifampicin, for only 11, including three with purpura, was treatment with the drug terminated. These adjustments were made entirely on the basis of the patients' clinical signs and symptoms and without any reference to antibody titres. Similar results have been reported from other centres.^{7,8}

Though the rifampicin-specific indirect antiglobulin reactions obtained with the serum of some patients with adverse reactions to intermittent rifampicin probably indicate the presence of circulating antibodies to the drug, this cannot be assumed.^{9,10} Nor, if such antibodies are present, can it be assumed that they are directly responsible for the reactions.^{2,11} Though the association between the occurrence of reactions and the presence of presumed antibodies has been shown to be close ($P < 0.002$), it is by no means absolute.^{6,10}

The assertion that "antibody titres within 24 hours after administration of the drug must be measured to find when they are lowest . . . and when a further dose may be safely given" is unjustifiable. An association between "antibody" titre and severity of reactions has not yet been clearly demonstrated. Even if it had, such measurements would be quite unnecessary in clinical practice since adverse reactions to intermittent rifampicin, as indicated above, can be managed simply and rapidly on an entirely clinical basis. However high the "antibody" titres in the serum of patients with reactions, rifampicin administration can almost invariably be continued uneventfully and without risk on a daily basis.^{1,6}—We are, etc.,

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Influenza in Families.

SIR,—A large-scale, five-year study of influenza in families in England and Wales began in October 1973 following a pilot trial in the previous winter. The study, organized jointly by the Royal College of General Practitioners and the Public Health Laboratory Service (P.H.L.S.), has nearly 500 volunteer patients. Over 50 general practitioners are taking part, each collaborating with one of 25 P.H.L.S. laboratories. The first winter period (1973-4) has run successfully and it has been decided to enlarge the study. Practitioners interested in taking part are invited to contact Mrs. J. Mant, Epidemic Observation Unit, Royal College of General Practitioners, 14 Princes Gate, Hyde Park, London SW7 1PU by letter or telephone (01-584 6262, ext. 43). At present it is not possible to include more general practitioners in the London area, but doctors from all other parts of England and Wales where laboratories are not already fully committed are welcomed.

Each doctor recruits between two and five volunteer families whose members will agree to provide a 10-ml blood sample in October and April each year (blood samples are not taken from children under 15 years). The families are kept under surveillance and each member is asked to contact the doctor if he develops an illness in which the diagnosis of influenza is even a remote possibility. The doctor or a nurse then records the clinical details and collects a nose and throat swab to be cultured for influenza viruses in the P.H.L.S. laboratory with which the doctor collaborates.

The main aims of the study are: (1) To relate pre-existing immunity, as measured by serological tests, to the influenza attack rate caused by new influenza virus strains as they naturally occur. (2) To study the relationship of pre-existing immunity to the severity of clinical influenza and to occurrence of subclinical infection. (3) To determine how influenza spreads within families.

The findings are expected to be of considerable practical importance. For instance, the results should help to improve the accuracy with which influenza epidemics could be forecast and help to decide when vaccination should take place and which persons should be included.

This is a worth-while study which can be carried out only by the close collaboration of general practitioners with their colleagues in virus laboratories.—I am, etc.,

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Computer Assisted Tomography

SIR,—In your leading article (22 June, p. 623) in which this most promising new method of investigating the intracranial soft tissues is reviewed the following statement regarding its application to the investigation of the orbit is made: "Various contrast media have been used in the past with very qualified success, and the techniques, apart from orbital phlebography, are regarded by most radiologists as being too dangerous since the information provided is limited." In our opinion this is misleading and totally

ignores recent contributions to the literature from a number of centres.¹⁻⁴ The implications are that current radiological techniques of orbital investigation are dangerous and inaccurate and that computer assisted tomography (E.M.I. scan) will supersede them.

In the Orbital Clinic at Moorfields, which is the largest clinic of its kind in Europe, we investigate over 150 patients each year and our preoperative diagnostic rate using current techniques is over 90%. We are at present engaged in an evaluation of computer assisted tomography of the orbit, comparing it with existing techniques; these include orbital venography, axial hypocycloidal tomography (Polytome), and ultrasonography (B-scan and holography). The latter two examinations are harmless, non-invasive techniques and are as well tolerated by the patient as computer assisted tomography. The preliminary results of this study, in which to date 17 patients in the series have had a lesion in the orbit verified surgically and histologically, shows an accuracy of preoperative diagnosis for computer assisted tomography of 76.5%. This compares with orbital venography 76.5%, axial hypocycloidal tomography 75%, and ultrasonic examination 62.5% in the same group of patients.⁵ It should be emphasized that a combination of these techniques was required for successful preoperative diagnosis in all cases, and in this respect the two most complementary procedures were orbital venography and ultrasonography. In addition, carotid angiography is still required in selected cases for complete diagnosis; this is particularly true of vascular lesions in the orbit, which make up 20-25% of orbital disease in the patients we investigate.

In the present state of development of the E.M.I. scan we feel that it is unlikely entirely to replace existing techniques. Positive contrast orbitography, which is presumably the dangerous method referred to, requires no replacement since it has long been discontinued in most centres because of the danger of optic nerve damage. The E.M.I. scan is complementary to existing procedures, and the results of our study show that we are in no way likely to abandon any of the methods listed above. This remains true in spite of the use, in the later E.M.I. scans in the series, of a prototype fine matrix system (Dr. J. A. E. Ambrose), which has improved the quality of the scans enormously and, in particular, has brought optic nerve abnormalities well within the diagnostic range of the apparatus.

Without wishing to detract in any way from the excellence of the results of orbital investigation which we have obtained using computer assisted tomography, we feel that it is premature to abandon accepted procedures on evidence from centres which perhaps do not always employ the full range of modern investigative techniques in the work-up of patients with suspected orbital tumours.—We are, etc.,

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¹ Vignaud, J., Clay, C., and Bilaniuk, L. T., *Radiology*, 1974, 110, 373.

² Lloyd, G. A. S., *British Journal of Radiology*, 1971, 44, 373.

³ Lloyd, G. A. S., *Transactions of the Ophthalmological Society of the United Kingdom*, 1973, 93, 301.

⁴ Coleman, D. J., Jack, R. L., and Franzen, L. A., *Archives of Ophthalmology*, 1972, 88, 358.

⁵ Ambrose J. A. E., Lloyd, G. A. S., and Wright, J. E. (to be published).

*Dr. Lloyd and Mr. Wright seem to be criticizing their own misinterpretation of our leading article. They quote articles concerned with hypocycloidal tomography and ultrasound, but these are not really relevant. Both techniques can be applied to the brain as well as the orbit and neither uses a contrast medium; ultrasound does not even employ x-rays. One of their references concerns phlebography, which the leading article accepted as being safe.

The article did not say, and we hope did not imply, that current ophthalmological radiological techniques are dangerous and inaccurate. We drew attention to the dangers of the past, as indeed do Dr. Lloyd and Mr. Wright in the second sentence of their penultimate paragraph. As far as radiological inaccuracy is concerned, we gave no figures for either the orbit or the brain.—ED., *B.M.J.*

Nursing Staff and Work Load

SIR,—The sudden influx of several major problem patients to one ward is a recurring problem of increasing seriousness as the progressive patient care concept deprives all but the intensive care unit of more than skeleton staff. Such cases do not always justify admission to the intensive care unit, which may in any case be full.

An example of this occurred recently in the burns unit of the South West Region, where the estimated work load doubled in three days and remained at this level for three months. The position was aggravated by a multiresistant staphylococcus infection which appeared on several of the major burns within a few days of their admission. In addition, the ward sister's annual leave commenced as the influx began, members of the nursing staff developed boils due to these organisms, and influenza caused further reduction of trained personnel.

It was considered that the volume of work represented by the three major burns was such as to justify an intensive care level of nursing and, as obviously the burns could not be cared for in the intensive care unit of the hospital because of their infections, eight beds in one arm of the 22-bed unit were closed, leaving the three major burns on the "dirty" side of the ward. Over the next eight weeks these patients were grafted and discharged or transferred.

We feel that this episode exemplifies the problems of modern medicine and nursing, which can be summarized as follows:

(1) Wards are being run on the absolute minimum of staff.

(2) When their work load snowballs, it will almost never be possible to supplement them from other wards.

(3) If the pressure is kept up by continuing admissions the work load is intolerable. Physical illness and severe reduction in morale follows. If continued, resignations are likely to follow, thus increasing the work load yet further. Mistakes could be made and patients suffer neglect.

(4) The only solution is to estimate regularly not the bed state but the work load, and reduce the bed state officially to match the available staff.

It is probable that this cannot be done objectively by the ward sister, who is in the thick of it.

(6) The Salmon system has provided a

person of experience to integrate and supervise small groups of wards. It would seem to be a most valuable function for her to assess the work load daily and initiate discussion and action with the doctors and administrators concerned leading to modification of the bed complement of the ward as often as is necessary.

(7) In this way the nursing staff might enjoy a tolerable balance between gross overwork and almost equally demoralizing under-employment.—We are, etc.,

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Accidental Injection of Potassium

SIR,—All medical graduates are surely aware of the risk of cardiac arrest if potassium is injected intravenously as a large bolus. Ten-millilitre ampoules of potassium chloride solution are currently produced looking very similar to ampoules of water for injection and normal saline. At least one firm has identical colours (green and white) on the boxes.

Several times I have observed drugs for intravenous use being dissolved in error in potassium chloride instead of water for injection. The mistake has been recognized by rechecking the ampoule before the injection was given. Colleagues of mine have known incidents in which potassium chloride solution has been used in error to dissolve antibiotics and to flush blocked intravenous cannulas, with immediate death resulting. Intravenous injections should be carefully checked (preferably by two people), but in emergencies and where understaffing is extreme this may not happen.

Is there not a case for potassium chloride, one of the most instantly fatal of poisons, to be in a coloured solution or in coloured ampoules?—I am, etc.,

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Contraceptives and Health

SIR,—The conclusions of the interim report on this subject by the Royal College of General Practitioners¹ that "adverse effects associated with the use of the pill are rare and that poor continuation rates could and should be greatly improved" are surprising in view of the evidence presented in the report.

There were statistically significant increases in the incidences of about 60 conditions among the 23,611 pill takers when compared with 22,766 controls. These were mostly mood changes, vascular disorders, some infections, and allergic disorders. It is noted that a variety of vascular diseases taken together suggest that the pill may affect small vessels and perhaps enhance neurovascular sensitivity. The findings of the Council for the Investigation of Fertility Control trial relating endometrial arterioles and sinusoids to clinical effects are overlooked.^{2,3}

During the four years of the survey