The conclusion is drawn that the ferrule of the umbrella passed below the level of the floor of the anterior cranial fossae and did not penetrate the dura of the right middle cranial fossa in view of the absence of cerebrospinal fluid rhinorrhoea. Anticipated vascular complications due to the lodgement of the tip of the ferrule near the posterior end of the contralateral cavernous sinus have not so far developed.

The pathological report reveals no direct injury to the globe of the left eye, which had been displaced into the lacrimal fossa. This fact could not be appreciated at the time of the operation, which required the sacrifice of that eye for reasons of urgent surgical access. The case demonstrates the need for careful investigation and the need for precautions in the management of deeply penetrating orbital injuries.

It is a pleasure to thank Mr. G. K. Burr, consultant ophthalmologist, for referring the case; Professor Norman Ashton, Institute of Ophthalmology, University of London, for the pathological report and guidance to the literature; and my associates for their assistance.

—I am, etc.,

H. H. GOSSMAN.

Plymouth General Hospital,
Plymouth.

REFERENCE

- 1 Lawson, G., *Injuries of the Eye, Orbit, and Eyelids*, 1867. London.

Liquor Bilirubin Levels

SIR,—I would like to make one point in connexion with the article by Mr. E. D. Morris and others (6 May, p. 352) on the use of liquor examination in Rh isoimmunization. When considering the significance of the liquor bilirubin level it is very important to take into account the stage of gestation at which this was carried out as the bilirubin level tends to fall as pregnancy advances. Our conclusions concerning the value of "liquor ratio" in predicting stillbirth are based on tests carried out at 34–36 weeks' gestation and the same level would not be expected to be applicable prior to 30 weeks, the stage of gestation at which most examinations referred to in this article were carried out.

The pattern of liquor bilirubin during pregnancy is illustrated in the following Figure which represents 11 Rh-negative preg-

gestation when selection of patients for intra-uterine transfusion might be contemplated.

The "exception" at 34 weeks illustrates one important source of error in liquor examination. At the initial tap a small amount of blood was aspirated which subsequently proved to be foetal in origin. The needle was repositioned and liquor obtained, but in retrospect it is probable that the small amount of foetal serum, with its high protein and bilirubin content, in a small volume of liquor would produce a very large error. It is therefore important that when serious contamination with blood occurs any sample of liquor should be discarded and a fresh one be obtained.—I am, etc.,

W. WALKER.

The Royal Victoria Infirmary,
Newcastle upon Tyne.

SIR,—The estimation of bilirubin in liquor amnii from Rhesus-positive women by Mr. E. D. Morris and others (6 May, p. 352) is of great interest in establishing the "normal" range, and they have apparently improved the value of these estimations by relating the concentration of bilirubin to the protein content and, presumably, to the volume of the liquor amnii. Results were expressed as a ratio $\frac{\text{bilirubin } \mu\text{g./ml.}}{\text{protein mg./ml.}}$, but they might be more easily understood if expressed as $\mu\text{g. bilirubin per mg. of protein}$, and I would like to suggest that results are written in this manner, if protein estimations are to become a usual part of the assessment of Rhesus-sensitized pregnancies.

There are both chemical and spectrophotometric methods in general use at present for the estimation of bilirubin in liquor amnii. The chemical methods have the advantage of giving quantitative results,¹ but it has been the experience of some workers that spectrophotometric methods demonstrate minor changes in pigment concentration more accurately.² Unfortunately, spectrophotometric methods give erroneous results unless corrections are made for contamination with haemoglobin. Scott³ and Alvey⁴ subtracted the optical density (O.D.) at a peak of absorption by oxyhaemoglobin (O.D. 574 $m\mu$) from a peak of absorption for bilirubin (O.D. 454 $m\mu$), but as the ratio $\frac{\text{haemoglobin O.D. 574 } m\mu}{\text{haemoglobin O.D. 454 } m\mu}$ is not unity, but approximately 0.75, the correction is not wholly accurate. The O.D. of haemoglobin at 490 $m\mu$ and 520 $m\mu$ is approximately the same, and the difference of O.D. at these two wavelengths can be taken as due to bilirubin alone,⁵ but Mr. Morris and his colleagues and other workers⁶ have not found this method satisfactory, possibly because of the rising curve of O.D. of turbidity and other pigments between these two points. The same errors enter the method of Liley,⁷ who calculates the O.D. 454 $m\mu$ over a baseline drawn from O.D. 550 $m\mu$ to O.D. 365 $m\mu$. The spectrophotometric method of Fleming and Woolf⁸ incorporates correction factors for turbidity, methaemalbumin, and oxyhaemoglobin, and I have found that the same bilirubin result can be obtained after heavy contamination of specimens with haemoglobin in vitro.

The estimation of the concentration of bilirubin in liquor amnii still needs refinement as a diagnostic tool, and a method would be preferable which expressed results as bili-

rubin, not as a ratio or an optical density figure.—I am, etc.,

A. F. FLEMING.

Department of Obstetrics and Gynaecology,
King Edward Memorial Hospital for Women,
Subiaco, Western Australia.

REFERENCES

- 1 Watson, D., *Proc. Ass. clin. Biochem.*, 1962, 2, 81.
- 2 Walker, A. H. C., and Jennison, R. F., *Brit. med. J.*, 1962, 2, 1152.
- 3 Scott, P., *A.C.B. Newsletter*, November, 1959. Cited by Savage *et al.*, 1966.
- 4 Alvey, J. P., *Amer. J. Obstet. Gynec.*, 1964, 90, 769.
- 5 Knox, E. G., Fairweather, D. V. I., and Walker, W., *Clin. Sci.*, 1965, 28, 147.
- 6 Savage, R. D., Walker, W., Fairweather, D. V. I., and Knox, E. G., *Lancet*, 1966, 2, 816.
- 7 Liley, A. W., *Amer. J. Obstet. Gynec.*, 1963, 86, 485.
- 8 Fleming, A. F., and Woolf, A. J., *Clin. chim. Acta*, 1965, 12, 67.

Narcosis for Chronic Tension

SIR,—Dr. William W. Sargent's statement (27 May, p. 573), "Meanwhile, I remain satisfied that there are, in this country and elsewhere, many hundreds of still well-preserved patients, many of them in the back wards of our mental hospitals, who would be greatly helped if they could only be given combined narcosis, E.C.T., and drug treatment—provided only that, prior to their long illness, they were able to cope with life's ordinary stresses," should not be allowed to pass without strong protest.

Such a statement, I feel, could be the cause of much distress to the staff of our mental hospitals and to relatives of patients who may happen upon it. No doubt every doctor has his professional failures, and, working in a teaching hospital, Dr. Sargent probably sees many of the failures of treatment by colleagues working in mental hospitals. Those of us who work in mental hospitals also see the failures of treatment in patients coming from teaching hospitals and professorial units.

If generalizations have to be made, in most psychiatric units physical treatments are given, if anything to an excess, as they are sometimes used as a substitute for the understanding and adjustment of the personality of the patient. Surely the main reason for failure in the treatment of "good-prognosis patients" in all psychiatric units is the lack of a healing personal contact between the patient and his physician, nurse, and relatives.—I am, etc.,

Powick,
Near Worcester.

G. I. TEWFIK.

Neurotoxic Effects of Piperazine

SIR,—There are few reports in the British literature on the neurotoxic effects of piperazine, and this case is therefore thought to be of interest.

A girl of 4 years 5 months was admitted to hospital on 15 January 1967, her mother giving the history that since awakening that morning the child had been unable to stand or sit without falling over. There was no previous history of ill-health except for a threadworm infestation, for which, for the two days before admission, she had received from her family doctor piperazine citrate, 1 teaspoonful (500 mg.) three times a day. Examination showed a small child whose weight at 12 kg. and height at 92 cm. were both under the 3rd percentile. She was afebrile but

nancies in which at least three liquor examinations were carried out. After 31–32 weeks the ratio with one exception was always below 1.06, but prior to this high values were found, especially before 25 weeks, a stage of

appeared disorientated and could not communicate. She was quite unable to stand or sit without falling over, and could not hold a cup to feed herself owing to frequent and repeated myoclonic jerks of her head and limbs. No other neurological abnormalities were found and general examination was normal. Lumbar puncture revealed no abnormality. Twenty-four hours after admission she was perfectly well.

The piperazine dosage was slightly in excess of that recommended by the manufacturers and it is probable that overdosage contributed to the toxic neurological signs. The frequency of reports of piperazine neurotoxicity in the Continental literature has been explained¹ by the use of the highly soluble piperazine hexahydrate, as opposed to the less soluble piperazine salts which are prescribed in Britain. Schuch *et al.* noted that a higher incidence of abnormal electroencephalograms occurred in children on therapeutic doses of piperazine hexahydrate compared with the less soluble piperazine tartrate, and thought that neurotoxicity was a true side-effect and not necessarily due to overdosage. They showed that children with neurological lesions or abnormal E.E.G.s are particularly at risk during piperazine therapy, and other authors are in agreement with them.²

Theoretically the less soluble piperazine salts should have a lower incidence of neurotoxicity. Of the salts available piperazine adipate is the least soluble and is known to be an effective anthelmintic. To date there have been no reports in the literature of neurotoxic side-effects from the use of this particular preparation, and it should perhaps therefore be prescribed in preference to the more soluble piperazine citrate which is used in some quantities in Great Britain.—I am, etc.,

D. C. L. SAVAGE.

Department of Child Health,
University of St. Andrews,
Scotland.

REFERENCES

- ¹ Schuch, P., Stephan, U., and Jacobi, G., *Lancet*, 1966, **1**, 1218.
- ² Snoeck, J., and van den Brande, J. L., *Maandschr. Kindergeneesk.*, 1965, **33**, 34.

Heroin Addiction

SIR,—Your correspondents Dr. G. G. Gray and Dr. P. A. L. Chapple (22 April, p. 246) draw attention to the proposed compulsory notification under the Dangerous Drugs Bill, 1967, of heroin addiction.

Such an enactment could present a serious challenge to medical psychotherapists because it would generally destroy the right of a medical psychotherapist to treat confidentially any patient who was a heroin addict. Apparently a non-medical psychotherapist would not be subject to this law and confidential treatment could be obtained from him. The medically qualified psychotherapist will be in a very difficult position because if he claims to treat patients in confidence and discovers that one of his patients is an addict he must either break faith with his patient or else he will be liable for the £1,000 fine or the 10 years in prison—for doing his duty. This is unfair both to the psychotherapist and to the patient. Surely the law should operate only in the case of a doctor who prescribes or arranges for the prescription of drugs for

an addict. And isn't the severity of the penalty in that order of things which we tend to condemn in those States which impose such penalties for political offences?

Furthermore, once this measure has been established it may be extended not only to other forms of addiction but possibly to other forms of antisocial behaviour which may come to the psychotherapist's notice.—I am, etc.,

Uffculme Clinic,
Birmingham 13.

D. T. MACLAY.

Compulsory Treatment of Addicts

SIR,—Dr. N. C. Lendon seems to be making the quite common mistake of confusing both drugs and motives (13 May, p. 444). Amphetamines are peddled in order to make money, while heroin is usually sold in order to survive; but in any case Dr. Lendon's "kindly compulsion" of 20–40 years' imprisonment is not one I think we shall see in this country. Dr. M. M. Glat's encouraging letter (13 May, p. 444) I think refers to addicts being compulsorily admitted to a unit comprising a number of patients who want to get off drugs. A new arrival, although initially negatively motivated, is quite likely to adopt the positive motivation of his peers. However, if the peer group inside hospital is negatively motivated—and this may happen if the majority of its members are being forcibly subjected to treatment—the chances of a new arrival being able to get off drugs is probably diminished.—I am, etc.,

Cane Hill Hospital,
Coudson, Surrey.

H. DALE BECKETT.

Conference on Tropical Medicine

SIR,—May I be permitted to remove a misunderstanding that has crept into the report of the Conference on Tropical Medicine recently held at the Royal College of Physicians, London? (17 June, p. 759). The sentence about the duration of treatment for leprosy should read: "Whatever the drug given, the total length of treatment advised is: in tuberculoid (and indeterminate) leprosy—at least two years, or one year after all clinical signs of activity have ceased; in multibacillary leprosy (lepromatous and borderline)—at least four years, or two years after all clinical and bacteriological evidence of activity have disappeared."—I am, etc.,

S. G. BROWNE.

London W.1.

Glycosuria in Pregnancy

SIR,—I would like to offer one or two observations on the article of Dr. J. Fine (28 January, p. 205). Both this paper and Dr. Fine's previous one (8 May 1965, p. 1209) rest entirely on the accuracy of the glucose oxidase-peroxidase technique normally used for estimating blood glucose being equally accurate in urine. In my opinion this is not so, for several reasons. My major

point is that filtering through charcoal alone removes some glucose from urine, or indeed from a pure glucose solution. Secondly, this filtering does not remove all colour or enzyme inhibitors.

The two main articles quoted^{1,2} are concerned with the estimation of glucose in blood and cerebrospinal fluid and mention urine but briefly. Marks² is a little more detailed, but even so his use of acid-washed activated charcoal is a quotation from J. D. Teller, and he points out that the resulting filtrate often has a pH low enough to affect the buffering activity of the enzyme solutions. The table he gives for glucose recovery after such filtration is "recovery almost complete," yet the scanty figures quoted are in fact only 88%, 78%, and 91%. This raises an important point in that Dr. Fine does not say whether his figures are the result of direct observation or of an added glucose recovery technique.

I have been concerned for some time with urinary glucose estimations, as I wished to pursue the work of Joplin, Fraser, and Keeley³ describing a prednisone-glycosuria test for prediabetes. My experience is that filtering a pure glucose solution alone through activated charcoal can remove some of the glucose. This can be shown by using a polarimeter with a 190.9 mm. tube giving 1° rotation for each 1% of glucose. The Hartnack machine is accurate to 0.05° and will thus detect 50 mg./100 ml. Thus, an estimation of glucose independent of enzyme activity was possible where the only variable was the filtration effect. Recovery varied between 75% and 85%, but never more, using a 1% solution. Even if one accepted that activated charcoal removed all colour and enzyme inhibitors, therefore, recovery would still not be complete. It can also be shown that ascorbic acid is not in fact completely removed, as this too is optically active, nor is urine colour completely cleared, even to the naked eye on occasion. Coming to the enzyme technique itself, it could be shown that one urine specimen, divided into many samples and estimated individually after filtration, gave widely varying results by direct estimation and by added glucose recovery technique. Here the time and temperature control during incubation proved to cause marked variations in the final result.

I would venture to say that for all practical purposes the glucose oxidase-peroxidase system is of no value in estimating down to the remarkably small degrees quoted by Dr. Fine—that is, 1–5 mg./100 ml. Too many sources for error exist. Apart from those discussed, there are the possibilities of peroxides being present from detergents on the glassware, etc., used for collecting the urine sample. Glutathione may be present in varying degrees in urine as well as ascorbic and uric acids. If the method is used at all I suggest that experimental variation alone could account for the hypoglucuric and hyperglucuric phenomena described.—I am, etc.,

T. LIND.

Princess Mary Maternity
Hospital,
Newcastle upon Tyne.

REFERENCES

- ¹ Huggett, A. St. G., and Nixon, D. A., *Lancet*, 1957, **2**, 368.
- ² Marks, V., *Clin. chim. Acta*, 1959, **4**, 395.
- ³ Joplin, G. F., Fraser, R., and Keeley, K. J., *Lancet*, 1961, **2**, 67.