changed and the indomethacin was replaced by phenylbutazone 100 mg., three times a day. On 29 March the prothrombin ratio was 2.7 and the dose of warfarin was reduced to 4.5 mg. per day. On 10 April he complained of spontaneous bruising on his hands and trunk. The prothrombin time was found to be 3.9, routine haematology proving normal. All drugs were stopped, no new purpura appeared, and seven days later the prothrombin ratio was 1.1.

Phenylbutazone had been prescribed six years previously for pain due to a lumbar disc lesion without any side-effects.

Brodie⁶ has drawn attention to the fact that several acidic drugs appear to compete for protein-binding sites. These drugs included tolbutamide, sulphonamides, and salicylates as well as the coumarins and phenylbutazone. Displacement of one such drug by another, giving increased unbound concentrations of the former at target sites, probably accounts for the potentiation of coumarins by pyrazole derivatives.⁷

The patient reported here did not develop haemorrhagic complications while taking indomethacin. However, this drug should also probably be used with circumspection in patients on coumarin anticoagulants in view of the similarity of its action to that of phenylbutazone in displacing protein-bound molecules.⁸—We are, etc.,

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Typhoid Fever—30 Years On

SIR,—I have recently encountered a case of a woman who has been a bacteriologically proved carrier of *Salmonella typhi* for 30 years. The records show she contracted typhoid fever in 1937, at which time it was not possible to clear up her carrier state. After several months in hospital, suffering considerably from the regimen of intestinal antiseptics that was then the only hope of eradicating the organism, she took her own discharge, still excreting *S. typhi*. She and her husband lived in a remote farmhouse some miles away from the nearest hamlet. The records state she refused to submit further samples of faeces. Her case was evidently lost sight of as the years went by, with no further cases of typhoid fever. Her children grew up and had children of their own, and the whole family regularly visited her to eat food that she prepared. It speaks well for the precautions she carried out that until this year no case of typhoid fever could be traced back to her.

Her carrier state came to light again when in January of this year her husband was admitted to hospital with atypical typhoid fever. His illness started in December with pyrexia, and after a few days he developed localizing signs of pneumonia. This failed to respond to antibiotics, and so he was admitted to hospital. There also his pneu-

monia and fever failed to respond to antibiotics. As a routine investigation, to exclude brucellosis, etc., blood was taken for agglutinations, and it was found that he had a raised titre of agglutinins for *S. typhi*. This titre rose later in the illness, and the organism was grown from blood culture. Despite treatment with chloramphenicol and ampicillin, to which the organism was sensitive in vitro, he collapsed and died. During the whole of his stay in hospital he had no diarrhoea.

All his close contacts were examined, and his wife was once again shown to be carrying the organism. Fortunately none of her many family contacts developed the disease, and tests showed there were no other carriers in the family. Remembering her unfortunate experiences of hospital treatment in 1937, she refused to go into hospital, but so far she has produced several negative faeces and urine samples after treatment at home with ampicillin and probenecid.

While 30 years of carrying *S. typhi* is probably not a record, a case where in 30 years only the carrier's closest contact, her spouse, has been infected seemed sufficiently unusual to report.—I am, etc.,

Spalding, Lincs.

J. M. MORFITT.

Penetrating Wound of the Orbit

SIR,—Penetrating wounds of the orbit are rare in civilian practice. An umbrella ferrule caused the death of a patient in 1866, described by Morgan, quoted by Lawson.¹ This report describes the successful removal of the ferrule of an umbrella from the left orbit.

A 24-year-old male patient attempted to settle an argument by force late in the evening of 17 December 1965, resulting in admission to the Plymouth neurosurgical unit. On examination the left palpebral fissure was seen to be completely filled by the foreign body. The patient retained full consciousness and was able to give an account of himself. The right pupil reacted normally to light and accommodation. The only abnormal neurological signs were complete right fifth and sixth nerve palsies. Plain radiographs of the skull showed the position of the foreign body (Figs. 1 and 2). Angiography carried out under general anaesthesia seven hours after admission demonstrated a very slow circulation through the right carotid tree. The antero-posterior projection of the left carotid angiogram revealed the path of the object across the midline, in addition to the demonstration of a nearly complete cross-circulation from left to right confirming that the flow through the right internal carotid artery was partially obstructed at the level of the cavernous sinus.

The ferrule (10 cm. long) was removed completely in one movement by twisting it in an anti-clockwise direction out of the left orbit. Towards the end of this manoeuvre the anaesthetist reported a marked fall in the patient's blood pressure and a severe haemorrhage through both nostrils took place. The right common carotid artery, exposed at the start of the operation, was occluded. The globe of the left eye was rapidly enucleated in order to pack the track of the foreign body with gelfoam. Pressure applied was withdrawn after 10 minutes, and since no further bleeding occurred the temporary occlusion of the right common carotid artery in the neck was released. The operation was concluded within the hour.

Recovery was uneventful. Three months later the patient returned to work. Minimal hypoaesthesia of the ophthalmic division of the right fifth nerve and a partial paresis of

the right sixth nerve were the only neurological signs. Sensation of the tongue had returned to normal.

Examination of left eye showed that the optic nerve was avulsed, but there was no external evidence of other injury. (In the author's opinion this "avulsion" was surgical and not traumatic.)

The microscopic report was: "Sections show avulsion of the optic nerve and there is mild cellular infiltration in the episclera. A little haemorrhagic and cellular debris is present in the anterior chamber and the epithelium of the iris and ciliary body on one side is disrupted and disorganized. A few chronic inflammatory cells are seen in the uvea and there are cystoid degenerative changes at the periphery of the retina, but otherwise the eye shows no obvious abnormality."

FIG. 1.—A preliminary plain x-ray of the skull, lateral view, prior to angiography.

FIG. 2.—Left carotid angiogram, arterial phase, antero-posterior projection, demonstrating the almost complete cross-circulation from left to right, with the path of the ferrule obliquely across the midline.

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.,

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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 immunization. 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.,

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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.,

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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