Depressive Illness in General Practice

SIR,—It is with interest one reads the paper by Dr. A. M. W. Porter on depressive illness in a general practice (28 March, p. 773). While Dr. Porter has put a lot of hard work into his paper, I feel it would have been valuable to enlarge on the parameters of the rating scales in order to bring out the important clinical assessment of depression such as external stress factors (reactive) and whether the depression is worse in the mornings. Is there sleep disturbance? Are there associated guilt feelings? Is there weight loss and poor appetite, and, most important, were there associated suicidal feelings? Stressing these clinical aspects would, I feel, have added more evidence to his conclusion.

I think it would also have been helpful to know what part psychotherapy played in the treatment and assessment, as it is important not to dissociate medication from psychotherapy even in clinical trials.

I feel it is a drawback that the duration of the trial was three weeks only. The conclusions arrived at might have been more significant if the duration of the trial was more than three weeks, since the Medical Research Council trial¹ showed that imipramine is a very worthwhile drug for treating depression. Dr. Porter indicated in his paper that in general practice quick results are expected. I think one would agree with him on this point so far as treatment of organic illness is concerned, but, with emotional illness, it takes certainly longer in view of the interactions of personalities and adaptation to stress factors, psychotherapy, etc.—I am, etc.,

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REFERENCE

- 1 Medical Research Council, *British Medical Journal*, 1965, 1, 881.

Supine Hypotension Syndrome

SIR,—Dr. L. Courtney (28 March, p. 797) has drawn the attention of obstetricians and anaesthetists to the risks of the supine hypotension syndrome to the mother at caesarean section. The death of one of the patients whose case history he describes underlines this point. Yet surely the adverse effects of supine hypotension on the fetus deserves some mention. It is likely that with either the fall in cardiac output or peripheral vasoconstriction that accompanies the condition there is a diminution in blood flow through the intervillous space. The extent to which uterine blood flow is affected is not known, but there is little doubt that fetal hypoxia is a common sequel.

During the course of continuous monitoring of the fetal heart rate in our intensive care labour ward at King's we have recorded acute fetal distress in five patients in the supine position, which was relieved by turning the patient on her side. The rapid improvement that accompanies this procedure is shown in the continuous fetal heart records obtained from two patients.

The patient whose record is shown in Figure 1 was known to suffer from supine hypotension, having had two attacks when placed in the lithotomy position prior to artificial rupture of the membranes. When labour started she was turned on to her back so that the midwives could record the fetal heart rate. Although she disliked this position, she was able to tolerate it. An irregular fetal heart rate was reported so a scalp electrode was applied to the fetus. The record shows an irregular bradycardia lasting 30 minutes. The pH of two fetal blood samples (F.B.S.) taken at this time was 7.20 and 7.18. The arrow shows the point when the patient was turned on her side, and an immediate recovery of the fetal heart rate to a normal level can be seen. The fetal pH 30 minutes later was 7.26.

The record in Figure 2 shows the change in fetal heart rate which was not accompanied by changes in fetal pH during a clinically more acute but shorter episode of supine hypotension than in the previous case. The patient, who was in the supine position, complained of feeling faint, became pale, and started to sweat. She recovered quickly as soon as she was turned on to her side. Figure 2 shows an episode of fetal tachycardia lasting three minutes followed by two minutes of profound bradycardia relieved by turning the patient on to her side.

Our experience of the beneficial effect to both mother and fetus of turning the mother on her side has encouraged us to try this simple expedient in all cases of fetal distress during labour. If, as a consequence, there is an improvement in the fetal heart rate pattern and pH labour is allowed to continue.—We are, etc.,

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Oral Lignocaine

SIR,—The paper by Dr. P. I. Parkinson and others (4 April, p. 29) was of interest to us as we have also carried out studies on the oral absorption of lignocaine in healthy volunteers. We are most surprised by the very high blood levels of lignocaine reported

by these authors, as such levels are unobtainable by similar dosages given by any other route, including intravenously. In the cases studied by us¹ 500 mg. orally gave maximum plasma levels of 1.2 µg./ml.—that is, one tenth of those reported by Dr. Parkinson and others. Plasma levels were determined by gas chromatography and were cross-checked by two independent laboratories, both with an extensive experience of plasma lignocaine estimations. Furthermore, the lignocaine blood levels in excess of 10 µg./ml. reported by Dr. Parkinson would be expected to give rise to convulsions or even coma.

We also noticed transient symptoms of toxicity in volunteers receiving oral lignocaine. These occurred at much lower plasma levels than has been observed with intravenous administration. We suggested that in its passage through the liver immediately following absorption the lignocaine was partially metabolized and that the metabolite was responsible for the toxic effects.

The anti-arrhythmic effects of oral lignocaine, reported by Dr. Parkinson and colleagues, are of interest, although it is extremely difficult to evaluate the anti-arrhythmic effects of orally administered drugs. If their observations can be confirmed, it suggests to us that the effectiveness of lignocaine by the oral route may be greater than can be accounted for by the plasma levels of lignocaine achieved. It is possible that such an anti-arrhythmic effect could be achieved by a metabolite of lignocaine.—We are, etc.,

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D. G. JULIAN.

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REFERENCE

- 1 Scott, D. B., Jebson, P. J., Godman, M. J., and Julian, D. G., *Lancet*, 1970, 1, 93.

Mefanamic Acid-induced Haemolytic Anaemia

SIR,—Dr. G. L. Scott and others¹ have reported three cases of haemolytic anaemia in association with mefanamic acid (Ponstan) therapy. The mechanism of red cell destruction appeared to be autoimmune in nature, similar to that described for methyl-dopa. The subject of immune drug-induced haemolytic anaemia has recently been reviewed by Worledge.² We report here haemolytic anaemia occurring in a patient with rheumatoid arthritis who was being treated with mefanamic acid, gold, and prednisone. An immune aetiology could not be detected.

The patient was a 50-year-old Caucasian male who had had rheumatoid arthritis for eight years. His previous drug treatment consisted of phenylbutazone, indomethacin, soluble aspirin, hydroxychloroquine, chloroquine, prednisone, and gold. In March 1967 he was receiving 10 mg. prednisone daily, and to this was added intramuscular sodium aurothiomalate (Myocrisin) every three weeks together with mefanamic acid (1.5 g. daily). This treatment was continued until his admission to hospital on 28 June 1969 with complaints of giddiness, tiredness, shortness of breath on exertion, nausea, and occasional vomiting. Haemoglobin was 7.4 g./100 ml.,

reticulocyte count 49%, and a film showed gross spherocytosis and polychromasia. The white cell count was 10,600/cu. cm. and the differential included 15% eosinophils. The spleen was not palpable. The direct antiglobulin (Coomb's) test was negative on three separate specimens; tests for Heinz bodies and abnormal blood pigments were negative, as also were Ham's acid-serum test, L.E. cells, G-6-P.D. and pyruvate kinase in red cells, the Donath-Landsteiner test, and haemoglobin electrophoresis. At the height of haemolysis, serum bilirubin was 1.9 mg./100 ml. and urinary urobilinogen was increased; the mean corpuscular fragility was increased, 0.48%. Both gold and mefanamic acid were ceased on admission, he was transfused and the haemoglobin concentration has since been normal, the spherocytes and reticulocytosis and eosinophilia having disappeared eight weeks later.

This case is of interest firstly as a report of a severe iatrogenic haemolytic disorder, and secondly in raising the possibility that mefanamic acid may cause haemolysis in the absence of an immune mechanism. It is not possible to be sure that the haemolysis was attributable solely to mefanamic acid. Gold compounds are well-known to have myelotoxic effects and also to cause eosinophilia, but we can find no record of their causing haemolysis. The possibility that gold had a combined or synergic effect with mefanamic acid cannot be excluded, but seems unlikely. Gold therapy has since been reintroduced in this case and so far no haematological abnormalities have developed.

Normal ABO-compatible red cells were incubated for varying periods of time in plasma and serum specimens taken during the haemolytic episode, but neither spherocytosis nor a positive antiglobulin (Coomb's) test was obtained. These experiments were performed with and without added mefanamic acid and complement.—We are, etc.,

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REFERENCES

- 1 Scott, G. L., Myles, A. B., and Bacon, P. A., *British Medical Journal*, 1968, 3, 534.
- 2 Worledge, S. M., *Seminars in Hematology*, 1969, 6, 181.

Erythromycin and Clindamycin

SIR,—Dr. I. Phillips and his colleagues (11 April, p. 89) suggest that clindamycin might be useful in treating patients with chronic purulent bronchitis. In vitro studies have shown that erythromycin is somewhat more active against *Haemophilus influenzae* and clindamycin against *Streptococcus pneumoniae*.

My colleagues and I have already shown in a controlled trial that erythromycin was significantly less effective than a tetracycline (lymecycline) or a novobiocin-tetracycline mixture (Albamycin-T) in treating patients with chronic purulent bronchitis.¹ It was especially poor in preventing clinical deterioration during and immediately after antibiotic treatment. From Dr. Phillips and colleagues' evidence it seems very unlikely that clindamycin will prove any better.

though both it and erythromycin might be useful in occasional patients.—I am, etc.,

A. PINES.

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Ware, Herts.

REFERENCE

- 1 Pines, A., Raafat, H., Plucinski, K., Greenfield, J. S. B., and Solari, M., *British Journal of Diseases of the Chest*, 1969, 63, 206.

Entonox in the Ambulance Service

SIR,—A small error in technical nomenclature has crept into our article on the use of Entonox in the ambulance service (4 April, p. 41) where, towards the end of the Discussion section, we refer to Entonox as being "inflammable."

Entonox is not an inflammable gas, and the sentence should read: "Though Entonox supports combustion, the danger of ignition is also more theoretical than real, since the gas mixture will flow from the cylinder only when a negative pressure is applied."

We should like to take this opportunity of recording that, since the above article was prepared, several other ambulance authorities are being equipped with Entonox apparatus.—We are, etc.,

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Protection from Sunlight

SIR,—Drs. R. M. Fusaro and W. J. Runge (21 March, p. 731) are to be congratulated on the efficacy of their dihydroxyacetone and lawsone cream in erythropoietic protoporphyria. We hope that their excellent results will be obtained by others.

Our paper,¹ to which they refer, was concerned with clinical and chemical study of a family and only incidentally with observations on two patients of the effect of dihydroxyacetone/lawsone lotion. The patients started treatment in 1964 according to the method described by Fusaro and Runge,² and which did not mention the instability of the ingredients when dispensed as a single mixture. The lotion comprised: dihydroxyacetone 3%; lawsone 0.035%; and isopropyl alcohol and water *ad* 100%; prepared freshly. Instructions were to apply to sun-exposed areas six times in the first day, then once daily to once weekly depending on the amount of sun exposure expected.

The patient observed most closely was the propositus—an indifferent witness who claimed to have less discomfort when using the lotion. This did not prevent development of new lesions or of progressive ageing changes. Using the monochromator, Dr. Ian Magnus was unable to demonstrate significant protection from 400 mμ wavelength in his skin pretreated with the lotion. The patient died of hepatic cirrhosis in 1969.

The second patient was aged 19 years and developed new lesions while using the lotion. He also claimed discomfort was reduced, and was sufficiently impressed to

ask for further supplies of lotion. It is probably true, as suggested by Drs. Fusaro and Runge, that these indifferent results were due to instability of the lotion used.

We are grateful to the authors for introducing an apparently effective cream for this most inconvenient and occasionally fatal disease.³—We are, etc.,

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REFERENCES

- 1 Donaldson, E. M., Donaldson, A. D., and Rimington, C., *British Medical Journal*, 1967, 1, 659.
- 2 Fusaro, R. M., and Runge, W. J., *Journal of American Medical Association*, 1962, 182, 1120.
- 3 Donaldson, E. M., *British Journal of Dermatology*, 1969, 81, 945.

"Adult Pink Disease"

SIR,—I have recently seen a number of patients with what can only be described as "adult pink disease" in south east Wales. It is characterized by erythroedema and polyneuropathy. The erythema, due to capillary dilatation, is noticeable in those parts of the skin exposed to the light, and, if marked, must give rise to a significant degree of arteriovenous shunting. The associated water retention gives rise to protean symptoms and signs, such as headache, vertigo, joint stiffness, and dyspnoea on exertion. The appearance of a neuropathy can lead to confusion with compression (entrapment) "neuritis," and could result in an unnecessary and unsuccessful operation for the relief of the supposed compression. Acroparaesthesiae, which are often present, seem to be related to the water retention.

Symptoms of respiratory tract irritation and even bronchitis, accompanied by gastrointestinal upset, suggest that the causal agent is airborne. There are good grounds for thinking that contamination of the atmosphere is the factor responsible, since patients recover in about two weeks without specific therapy if removed from this area. Attempts to have the problem investigated by expert agencies in air pollution have so far produced no response. Until this is done, it seems we may expect to see more and more cases of "adult pink disease."—I am, etc.,

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Mon.

The Ophthalmologist

SIR,—I understand that some distress has been caused among junior residents after your recent publication in the "Unheard Voices" series (28 March, p. 813). I would like to make it plain that my remarks were general and I was not thinking of any particular person. My present registrar is very competent and well able to take over clinics if I am on leave. Previously clinics have had to be cancelled partly due to the difficulty many overseas graduates, and indeed Englishmen, have in understanding the local dialect and expressions; also the junior staff are not always free to cover my clinics, nor