ment will be to encourage the new medical generation to take a positive role in the battle for the environment and to encourage the profession as a whole to adopt this role, which lamentably it has failed to do so far. As the doctors of tomorrow, today's medical students are not prepared to suffer the devastating consequences to health of today's environment.

In conclusion, the organizers of this symposium have asked me to express their whole-hearted support for the aims of those whose recent letter (8 January, p. 108) urged extensive action on the problem of population control. It is their hope that other members of the medical profession will be encouraged to do likewise.—I am, etc.,

PETER BERREY
Secretary, B.M.S.A.

South Bridge,
Edinburgh

Laxative Jaundice

SIR,—You say (5 February, p. 325) that cases of chronic active hepatitis associated with the use of oxyphenisatin are the first in which a drug has been implicated. Histological changes resembling chronic active hepatitis have, however, been recorded in two patients treated with methyl dopa,^{1,2} though the characteristic clinical and biochemical features were absent. We are at present preparing a report of four patients in whom the full syndrome of chronic active hepatitis appeared to follow the use of methyl dopa in two and the contraceptive pill in two. It is important that such patients be questioned carefully about drug taking including preparations used for self-medication.—I am, etc.,

A. PATON

Dudley Road Hospital,
Birmingham

- ¹ Morin, Y., Turmel, L., and Fortier, J., *American Journal of the Medical Sciences*, 1964, 248, 633.
² Williams, E. R., and Khan, M. A., *Journal of Therapeutics and Clinical Research*, 1967, 1, 5.

Herpes Encephalitis in Pregnancy

SIR,—We have recently had the opportunity to observe herpes simplex encephalitis in a young woman who delivered a live child during the course of her fatal illness. We believe the virological and histological findings strongly suggest direct neural transmission without viraemic spread.

A 19-year-old woman presented near term with a pharyngitis and pyrexia and during the next 10 days progressively developed dysphasia, right hemiparesis, hemihypaesthesia, hemianopia, and deterioration in conscious level. Technetium brain scan and left carotid arteriography showed a large left temporal space occupying lesion. Biopsy of this showed evidence of encephalitis and positive fluorescent antibody study to herpes simplex virus, which was subsequently cultured from ventricular cerebrospinal fluid and the biopsy. Treatment with intravenous idoxuridine, 2.5 g in 500 ml 5% dextrose 8 hourly was unavailing and she died two days later.

At necropsy the brain was swollen and there was necrosis of both olfactory bulbs and tracts and the left temporoparietal and hippocampal regions. Cowdry type A intranuclear inclusions were found in the right temporal lobe.

Five days before she died she was delivered of a live child, who remained healthy. No antibody to herpes simplex was demonstrable in his blood when he was 23 days old.

Buddingh *et al.*¹ found that in primary herpetic stomatitis neutralizing antibodies were first demonstrated in the serum from the fourth to the seventh day of the disease and that maximal levels were found during the second and third week. They also demonstrated transplacental transfer of antibody. Herpetic infection in neonates is frequently fatal whether or not circulating antibody is present. The absence of an antibody response in the mother together with the absence of antibody and clinical infection in the infant make it unlikely that the virus was spread by the bloodstream. As well as dissemination by blood, Johnson and Mims² demonstrated that virus could reach the central nervous system by spread across the olfactory mucosa and infection of endoneural or perineural cells. The necropsy findings of olfactory bulb, tract, and hippocampal necrosis together with virus isolation from temporal lobe lend support to the hypothesis that in this case the virus spread by the direct neural and not the haematogenous route.

Our previous experience with idoxuridine in herpes simplex encephalitis (admittedly small, four cases) has left us unconvinced of its therapeutic value. However, the present case was in such a critical condition at the time of administration that her death could hardly be attributed to lack of action of the drug.—We are, etc.,

J. M. ANDERSON
M. W. N. NICHOLLS

Midland Centre for Neurosurgery and Neurology,
Smethwick, Worcs

- ¹ Buddingh, G. J., Schrum, D. I., Lanier, J. C., and Guidry, D. J., *Pediatrics*, 1953, 11, 595.
² Johnson, R. T., and Mims, C. A., *New England Journal of Medicine*, 1968, 278, 23, and 84.

Hypothyroidism after Partial Thyroidectomy

SIR,—Mr. W. Michie and his colleagues (1 January, p. 13) report a 49% incidence of hypothyroidism in patients who had undergone a thyroidectomy up to seven years previously. From this data clearly a careful follow-up of these patients is essential. Their discovery that a serum P.B.I. at one and four months after operation gave an indication of the future status of the individual patient makes this investigation obligatory where a subtotal excision has previously been performed.

In a busy outpatient clinic the important clinical assessment of these patients may be passed to the junior staff after some months. For this reason, regrettably, the patient may well see a different doctor on almost every visit. Subtle changes in facial appearance may thus be missed unless photographs of the patient taken at the time of the original surgery are included in the notes. Mr. Michie states that in their cases neither clinical nor E.C.G. evidence of hypothyroidism was seen until three years post-operatively. However, comparison of the patients' features with a photograph taken at the time of surgery may allow much earlier clinical diagnosis of thyroidism—a useful adjunct to the biochemical data.—I am, etc.,

ROY E. MAY

Frenchay Hospital,
Bristol

Hyperpyrexia and Overdose

SIR,—We would like to record an unusual case of malignant hyperpyrexia associated with overdosage of fenfluramine.

A 34-year-old housewife with a long history of anxiety depression including many previous suicide attempts was admitted to our hospital with a history of having apparently taken 50 fenfluramine tablets. On admission she was drowsy but able to hold a conversation. However, over the next 20 minutes she became unconscious, began to hyperventilate, developed tachycardia, and began to sweat profusely. At this time she also went rigid, flexing her arms and legs and moving her forearms with irregular writhing movements. She also developed coarse rolling movements of the eyes in all directions.

She was given diazepam 10 mg intravenously, followed by 10 ml of calcium gluconate intravenously and 100 mg chlorpromazine intramuscularly, to no effect. At this point she was given succinylcholine, intubated, and artificially ventilated, as her breathing had become stertorous. Following this her rigidity disappeared, and within about 15 minutes her skin was noted to be hot and dry. Her rectal temperature on two successive readings was found to be 109°F (42.8°C). An attempt was made to reduce her temperature by conventional means, and it was decided to use procaine intravenously to treat her hyperpyrexia, as described by Harrison.¹ The patient was given an infusion of 5% dextrose saline with 60 mg of procaine as a loading dose. This, in fact, was only one-sixth of the recommended dose because, as the infusion started, her blood pressure dropped from 100 systolic to 70 systolic. She was then given a maintenance dose of 0.2 mg/kg/min of intravenous procaine over the next two hours. Isoprenaline was not given as recommended, because of her tachycardia of 180. Within about half-an-hour her temperature dropped to 90°F (33°C). Her blood pressure remained at about 70 mm/Hg systolic despite plentiful fluid replacement. During the subsequent hours her blood pressure became unrecordable and she died about 13½ hours after admission.

In four recorded fatalities² following fenfluramine overdose, all associated with overdosage greater than 90 tablets, there was a rise in blood pressure, hyperventilation, sweating, clonic convulsions followed by rigidity of the limbs, and usually a fatal cardiac arrhythmia. In all of these cases a high temperature was recorded. In one case of a 13-year-old child taking an overdose of fenfluramine the temperature went up to 107°F (41.7°C).²

We felt that the hyperpyrexia was due to fenfluramine overdosage rather than being succinylcholine-induced, because of the short space of time which elapsed between giving the succinylcholine and recording a temperature of 109°F (42.8°C). The maximum rate of rise in temperature in malignant hyperpyrexia is said to be 1°F per 5-10 minutes.³ One case in which procainamide has been used successfully in the treatment of malignant hyperpyrexia has been recorded.⁴ Procaine has been shown to give some benefit in treating Landrace pigs with hyperpyrexia.¹ Chlorpromazine⁵ has also been used in the successful treatment of malignant hyperpyrexia, and a review of the methods of treatment for this condition is in preparation.⁶ To exclude any hereditary myopathy which might have caused this alarming pyrexial response in this patient we are in the process of estimating creatine phosphokinase and aldolase in the sera of other members of this patient's family. In our case, procaine and conservative measures reduced the temperature very rapidly but the patient died, possibly because the blood levels were in fact extremely high and

compatible with a larger overdose than was originally suspected (probably about 100 tablets).

We would like to thank Dr. Philip Harvey for giving his permission to report this case and Dr. D. B. Campbell at the Guy's Hospital Poisons Centre for performing the fenfluramine level estimations.

—We are, etc.,

A. P. HAINES
P. J. SHOENBERG

St. Stephen's Hospital,
London S.W.10

- 1 G. G. Harrison, *British Medical Journal*, 1971, 3, 454.
- 2 Fleisher, M. R., and Campbell, D. B., *Lancet*, 1969, 2, 1306.
- 3 Furniss, P., *Proceedings of the Royal Society of Medicine*, 1971, 64, 216.
- 4 Beldavs Small, V., Cooper, D. A., and Britt, B. A., *Canadian Anaesthetists' Society Journal*, 1971, 18, 202.
- 5 Robertson, J. C., *Postgraduate Medical Journal*, 1972, 48, 64.
- 6 Robertson, J. C., personal communication.

Erythropoietin

SIR,—The useful leading article on "Erythropoietin" (29 January, p. 263) contains two points worthy of comment.

Firstly, "... there is not the expected increase in erythropoietin in the anaemias associated with uraemia and with protein starvation. . . ." If one assumes that in the case of uraemia the destructive kidney disease which causes uraemia also damages the renal source of erythropoietin, then a low erythropoietin level would be expected and might, at least in part, explain the anaemia.

Secondly, "A surprising discovery has been that erythropoietin levels are not increased in polycythaemia vera and may be actually lower than normal." There is evidence that polycythaemia vera is primarily a disease of the bone marrow in that (1) there is an increased rate of formation of granulocytes and thrombocytes as well as erythrocytes; (2) in some cases the disease progresses to leukaemia or myelofibrosis, and (3) cultured polycythaemia vera marrow is unresponsive to erythropoietin. The situation seems in some ways analogous to autonomous overactivity of an end-organ such as the thyroid or the adrenal cortex. In such cases, owing to negative feedback control, the level of the trophic hormone tends to be low. Similarly if in polycythaemia vera the end-organ (bone marrow) is spontaneously hyperactive, one would not expect an increase in the level of the hormone (erythropoietin) which stimulates it.—I am, etc.,

W. F. M. WALLACE

Physiology Department,
Medical Biology Centre,
Queen's University of Belfast

Pharmacologically Active I.U.D.s

SIR,—I am afraid that I must take issue with two letters on the subject of pharmacologically active I.U.D.s. Dr. R. M. Pearson (19 February, p. 508) states "The Dalkon shield . . . contains over 40% of its weight as barium sulphate." This statement is wrong, and the actual percentage of barium sulphate by weight in the Dalkon shield is between 10-11%. We have no evidence that any of the barium sulphate is actually leached out of the plastic matrix. The reason for such a small amount of barium being used during the manufacture of the

Dalkon shield is that it is possible by so reducing the amount of barium sulphate to come up with a plastic mould which is much more flexible and much more foldable than earlier plastic I.U.D.s.

My second comment is on the statement by Dr. M. Elstein and Miss Karen Ferrer (19 February, p. 507), who seem to be trying to suggest that the I.U.D. of increased surface area necessarily means a concomitant heavy prolonged bleeding problem. The basic design of the Dalkon shield with its lateral fins prevents this increase in bleeding though still presenting a large surface area of device to the endometrium, and it was specifically engineered with this aim in view. I have not yet received any reports of severe bleeding following on insertion of a Dalkon shield though, as is to be expected, a few women experience an increase in menstrual blood loss for the first one or two periods after insertion.—I am, etc.,

J. S. TEMPLETON
Medical Adviser,
A. H. Robins Co. Ltd.

Horsham, Sussex

Diazepam and Fentanyl Dosage

SIR,—We shall be grateful if you will draw the attention of your readers to a typographical error in a dosage chart in our *SAAD Digest* No. 9 (p. 194).

The Table referred to gave a milligram heading for both diazepam and fentanyl; the latter should, of course, have been microgram, not milligram. The text of the article made the correct dosage quite clear.

This error was traced to the typed cipher "ug" being mistaken for "mg" on a carbon copy, and with the increasing use of micro-

grams—and the ease with which typing errors can occur—a better official differentiation may avoid similar errors.—We are, etc.,

D. BLATCHLEY
Medical Editor

S. L. DRUMMOND-JACKSON
Dental Editor
SAAD Digest

London W.1

Abortion Figures

SIR,—If the author of your leading article (22 January, p. 193) had waited a few days, until he had seen the announcement of the Department of Health that 126,774 abortions had been carried out in 1971, he would, I am sure, have omitted his first paragraph. It read "A notable change in obstetric thinking in recent years has been a greater concern for the welfare of the fetus in utero."—I am, etc.,

J. P. G. ROGERSON

Whitchurch,
Shropshire

Apology

We much regret that because of a mistake in the *B.M.J.* office a letter from Dr. C. E. Astley, Chairman of the Central Committee for Hospital Medical Services (29 January, p. 315), was wrongly related to Mr. S. C. Simmons and to the debate which the C.C.H.M.S. held on 16 December (*Supplement*, 1 January, p. 4). Dr. Astley was replying to a letter by someone else, which was eventually withdrawn from publication. We regret our part in this misunderstanding and apologize to all concerned for the embarrassment we have caused them.—Ed., *B.M.J.*

Points from Letters

Use of Amphetamines by Drivers

Mr. A. G. BUTTERS (Barnsley, Yorks) writes: Dr. S. J. Carne's concluding remarks, "Those who cannot drive a car without a sedative or pep pill ought not to be driving at all" (12 February, p. 439) could well be amplified—for example, students who turn to a tranquilizing drug when faced with the ordeal of a forthcoming examination. One wonders as they are unable to face up to ordeals without an artificial aid how they will make out in the future. Are we reaching the stage when too many tranquilizers are being prescribed too freely, and has the time come to take a second look? Is it that our patients expect relief from their ailments by taking the latest tablet and not by making that extra effort themselves. . . .

Benzhexol and Long-acting Fluphenazine

Dr. G. R. DANIEL (Medical Director, E. R. Squibb and Sons Ltd., Twickenham, Middx) writes: It was interesting to read Drs. Lynn Grove and J. L. Crammer's article (29 January, p. 276) on the withdrawal of benzhexol from patients receiving fluphenazine enanthate. I believe the series of eight from whom medication was withdrawn was too small to make any judgement on the expected incidence of extrapyramidal reactions and need for anti-Parkinsonian drugs following prolonged therapy with the injections. Indeed, the high dose of fluphenazine enanthate used (up to 75 mg) as well as the high dose of benzhexol (up to 40 mg) indicates that the patient population was anything but typical. Of the four patients who

developed symptoms after withdrawal of benzhexol, one had diarrhoea, sweating, and malaise—a condition more reminiscent of enteritis than extrapyramidal symptoms. . . . A further point of consideration in a patient population of this kind is that before starting such a study it should be necessary to exclude those suffering from other forms of Parkinsonism and those with tardive dyskinesias, possibly associated with the chronic administration of phenothiazines over many years. . . . Most psychiatrists have now virtually abandoned fluphenazine enanthate for fluphenazine decanoate, which in practice clearly produces far less extrapyramidal reactions. . . .

Quality Control for Serum Phenytoin

Dr. A. RICHENS (Department of Clinical Pharmacology, St. Bartholomew's Hospital, London E.C.1) writes: May I use your columns to invite laboratories which are at present measuring serum phenytoin concentrations for routine or research purposes to join a scheme designed to produce a quality control for these estimations? A recent co-operative study between seven laboratories has shown considerable discrepancies in the results produced on identical samples and indicates a need for such a control. This will serve to make future published data strictly comparable. . . . The Committee of the Epilepsy Research Fund has an interest in this problem and we are supporting the work financially. Would anyone who is interested in this scheme please write to me?