

as safe as Dr Jackson-Moore believes them to be; they undoubtedly have great promise. Nevertheless, at the present time we would recommend for at-risk patients an up-to-date inactivated vaccine rather than live A/England vaccine.—ED, *BMJ*.

Thrombocytopenia during treatment with clonazepam

SIR,—We think it is desirable to publicise as a matter of some urgency a potentially dangerous thrombocytopenia developing probably as a reaction to the drug clonazepam (Rivotril).

The patient is a 52-year-old woman resident at a hostel for mentally subnormal women under the control of Botleys Park Hospital. She has an IQ of 55 and is able to carry on a useful conversation. There is a history of head injury at age 3 followed by epilepsy. There is no reliable history of her development before that. Until recently she had no epilepsy after childhood.

On 25 September 1974 while drinking morning tea at work she was noticed to be oblivious of her surroundings; her right hand was shaking and she was spilling her tea. She recovered completely in a few seconds. She had a similar attack the next day, another in October, and one in November. Investigations including blood glucose and calcium, lumbar puncture, and electroencephalography were negative. She was free of attacks until June 1975, when treatment with phenytoin 150 mg daily was started. She had further attacks and clonazepam 0.5 mg twice daily was added on 30 July. Following a further attack in August this was increased to 1.0 mg twice daily. On 5 September she had a mild epistaxis and two days later more severe epistaxis and purpura. She was admitted to St Peter's Hospital, where her nostrils were found to be blocked with clotted blood and she was bleeding from the lower gum, the upper being edentulous. Multiple purpuric spots and bruises were present on both legs. All drugs were stopped.

Examination of the blood showed a platelet count of $6 \times 10^9/l$ (6000/mm³), but was otherwise normal. A sternal marrow puncture the following day showed an excess of megakaryocytes and no other abnormality. Prednisone 20 mg three times a day was started. The puncture site continued to ooze for 2-3 days. Platelet counts performed on 8 and 10 September showed a fall to less than $1 \times 10^9/l$ (1000/mm³).

On 12 September the patient had a grand mal fit and was started on phenobarbitone 30 mg three times a day. On 19 September the platelet count had risen to $48 \times 10^9/l$ (48 000/mm³) and it was $64 \times 10^9/l$ (64 000/mm³) on 22 September and $152 \times 10^9/l$ (152 000/mm³) on 10 October. She is being followed up and her steroids will be reduced and stopped if she has no relapse.

There have been only two reports of thrombocytopenia attributed to phenytoin, although it is prescribed about a million times a year. No warning is given about thrombocytopenia as a reaction to clonazepam by the manufacturers (Roche). As a result of inquiries they have kindly searched the literature and have found one report by Girke *et al*¹ of a fall in the thrombocyte count in 9 of 26 patients being treated with clonazepam alone, with a minimum value of $90 \times 10^9/l$ (90 000/mm³). These changes were shown "to be reversible at check-ups." It is not stated how the changes were reversed.

The Committee on Safety of Medicines has been informed.

R M VEALL

Botleys Park Hospital

H C HOGARTH

St Peter's Hospital,
Chertsey, Surrey

¹ Girke, W, Krebs, F A, and Lenzner, W, *Ärztliche Praxis*, 1973, 25, 4518, 4520, 4522.

Treatment of meningitis and encephalitis

SIR,—I would question Dr C C Smith's choice of cephaloridine for treatment of penicillin-allergic patients with meningococcal infection (8 November, p 335). The organism can be relatively resistant to cephalosporins and there have been reports of poor clinical results of treatment with both cephaloridine¹ and cephalothin.² Furthermore, one needs to remember that cross-allergenicity does exist between the cephalosporins and the penicillins; from the worldwide clinical experience of using cephalosporins in penicillin-allergic patients the estimated risk of clinical reaction has been stated to be about 6-9%.³

As things stand at present the choice of drug in such cases should be chloramphenicol, although co-trimoxazole may turn out to be a safer alternative if the encouraging results from Africa⁴ can be confirmed in further studies.

B K MANDAL

Monsall Hospital,
Manchester

¹ McKenzie, P, *et al*, *Postgraduate Medical Journal*, 1967, 43, suppl (August), p 142.

² Southern, P M, and Sandford, J P, *New England Journal of Medicine*, 1969, 280, 1163.

³ Dash, C H, *Journal of Antimicrobial Chemistry and Chemotherapy*, 1975, 1, suppl, p 107.

⁴ Felix, H, *Revue de Médecine*, 1971, 23, 1503.

Abortion again

SIR,—In your leading article on abortion (1 November, p 244) you fail to discuss the most important principle—that the fetus is a human being—and its corollary—that its life should not be destroyed except to save the mother's life. Your underlying principle seems to be that abortion on demand is desirable, and I think it only fair that you give space in your columns for those opposing this view to state their case.

There are many doctors who treat the fetus as a human being who has as much right to our medical skills as any other person and who is not to be treated like a cancer, to be cut out and thrown away.

IAN EVANS

Swansea

Hazard of air embolism with multiple infusion apparatus

SIR,—In their short report (25 October, p 204) Dr R V Heatley and Mr B K Evans describe an apparatus designed to overcome the problem of multiple intravenous fluid infusion. When similarly trying to simplify the "plumbing" of just such regimens by utilising a common drip chamber and regulating the flow from each container by clamps above that chamber I have found experimentally that there is a serious risk of air embolism, whether or not a pump is used, if the drip chamber is at a height above that of the central venous pressure. If one bottle empties unobserved free entry of air to the common drip chamber will occur via that bottle's airway. The fluid level will then drop repeatedly into the line to the patient while the other drips continue, so that a flowing column of fluid and air enters the circulation. The higher the chamber, the faster the inflow. The fact that fluid from the other bottles continues to drip into the

chamber increases the likelihood that the attendant will fail to notice the empty bottle.

The potential hazard of air embolism can be avoided only by ensuring that the point where all the infusions come together, be it chamber, tap, or Y-connector, is at or below the level of the patient's central venous pressure.

STUART J TOVEY

Department of Nephrology,
Southmead Hospital,
Bristol

Poisoning with slow-release fenfluramine

SIR,—We wish to report the first death from ingestion of the 60-mg "slow-release" preparation of fenfluramine (Ponderax Pacaps, Servier). Deaths from earlier fenfluramine preparations have been reported previously.¹⁻⁴

A 5-year-old girl with a history of a febrile convulsion at 18 months told her mother that she had swallowed two Ponderax Pacaps half an hour earlier. Eventually 20 capsules (1200 mg, 70 mg/kg body weight) were found to be missing. On admission to hospital one hour after ingestion she was flushed, drowsy, dysarthric, and tremulous, with fine nystagmus. She could answer questions coherently. Her pulse and respiration rates were 116/min and 24/min respectively. Rectal temperature was 37°C.

Gastric lavage was carried out with the recovery of whitish material. Near the end of the procedure she had a tonic-clonic convulsion and was treated immediately with diazepam 5 mg intravenously. Convulsions ceased after two minutes, by which time she was limp and pulseless, with fixed, dilated pupils. After rapid endotracheal intubation, ventilation with 100% oxygen, and cardiac massage broad low-voltage complexes at 140/min were noted on the ECG. Despite resuscitative efforts, which included intravenous administration of sodium bicarbonate, calcium gluconate, 20% mannitol, and atropine, followed by intracardiac adrenaline and DC shock, she died some three hours after the ingestion of fenfluramine. Necropsy (by Dr R Nagle, Lothian and Borders police surgeon) showed mild congestion of the brain, slight pallor of the heart muscle, and whitish material in the stomach. Toxicological examination of the liver showed 2.4 mg of fenfluramine/100 g of liver.

In spite of the preparation being "slow-release" this history is typical of fenfluramine intoxication. Convulsions and cardiac arrhythmias have both been reported in fatal cases, the convulsions usually occurring first. In primates⁵ the parenteral administration of 50 mg/kg of fenfluramine causes convulsions and death some 90-240 min later. Cardiac arrhythmias and respiratory arrest occur terminally. Cardiac monitoring has been recommended by several authors and also the manufacturers of fenfluramine when toxicity is suspected. There have, however, been at least two fatal cases^{2,4} in which this precaution was taken.

In primates⁵ a lower convulsion threshold to various stimuli such as noise and handling has been observed. This suggests that syrup of ipecacuanha (*BPC*) used successfully in a child who had ingested 70 mg/kg fenfluramine⁶ might be preferable to gastric lavage. Other supportive measures used successfully in two 3-year-old children⁶ have included prophylactic intramuscular and intravenous diazepam. The reported deaths have occurred within three hours of ingestion and it has been inferred that recovery is likely if the child survives for four hours. Therapeutic doses of fenfluramine have been shown to cause mild hypoglycaemia,⁷

but the effect on glucose metabolism of severe intoxication has not been reported. In rodents glucose appears to enhance the toxic effects of fenfluramine, which suggests that it is unlikely to have a therapeutic role in severe intoxication in humans.

Although appetite suppressants cost the NHS over £2m in 1973, their efficacy in the long term remains somewhat dubious. Their dangers, however, even when individually wrapped, continue to be demonstrated.

HAMISH SIMPSON
IAN MCKINLAY

Royal Hospital for Sick Children,
Edinburgh

1 Gold, R G, *et al*, *Lancet*, 1969, 2, 1306.

2 Fleisher, M R, and Campbell, D B, *Lancet*, 1969, 2, 1306.

3 Stapley, M L, quoted by Campbell, D B, and Moore, B W R, *Lancet*, 1969, 2, 1307.

4 Veltri, J C, and Temple, A R, *Journal of Pediatrics*, 1975, 87, 119.

5 Kündig, H, *South African Medical Journal*, 1971, 45, suppl, p 11.

6 Darmady, J M, *Archives of Disease in Childhood*, 1974, 49, 328.

7 Turtle, J T, Burgess, J A, and Bauckhan, S, *South African Medical Journal*, 1971, 45, suppl, p 22.

Family planning prospects

SIR,—In your recent leading article (18 October, p 124) on family planning prospects you write that it would be a tragic irony if the well-intentioned State takeover of family planning clinics led to their decline rather than their expansion. Surely the reverse is true, and one can only hope that as more doctors become trained and proficient in family planning it would become once again an integral part of a general practitioner's duties, with consequent decline of the clinics. The tragic irony is that the FPA flourished only because the training of a generation of general practitioners left them unable to deal with this problem.

CHRISTOPHER TRANMER

Buckhurst Hill, Essex

SIR,—In your leading article Family Planning Prospects (18 October, p 124), you state correctly that the "FPA seems content to let the newly formed Institute of Psychosexual Medicine provide the training and specialised knowledge." There are, however, many doctors within and outside the FPA who feel that the aims of the institute are too limited in this very wide field of medical practice. Because of this the Society for the Study of Human Sexual Behaviour has been formed with particular attention to training and promotion of epidemiological studies.

As secretary of the society I would be very glad to help with further information for any who might be interested. Meetings are to be in Scotland and the north of England but members from all areas will be welcome.

LORNA D NAISMITH

9 Bocclair Road,
Bearsden, Glasgow

Experience gained in vocational training in obstetrics

SIR,—Recent discussions on the future of obstetrics in general practice¹⁻⁶ have debated the role of the Diploma of Obstetrics,^{1,2} the use of obstetric beds in a consultant unit,³

and claims for complete services,¹ but the actual experience gained in a six-month obstetric post has not been discussed. This is important, since it is this practical experience which determines a doctor's suitability to carry out the various tasks demanded in obstetric care.

To fill this gap we report the method of delivery in the 319 cases that occurred while one of us (AM) as a vocational trainee was on call during a six-month obstetric post. The nature and number of cases were as follows: normal, all stages 34; artificial rupture of membranes and spontaneous vertex delivery 185; brow presentation 1; face presentation 1; shoulder presentation 1; presenting occipitoposterior 4; stillbirths 12; breech presentation 15; mid-cavity forceps 36; Keilland's forceps 9; ventouse extraction 4; twins 2; manual rotation 1; caesarean section 14.

AM was not in attendance at all the deliveries, as normal deliveries were carried out by the midwives on duty at the time. We estimate that he took an active part in 70 of the recorded deliveries. Thus it may be seen that though he applied mid-cavity forceps and carried out breech deliveries his experience of other forms of abnormal presentation was very limited. It may be postulated that the number of normal vertex presentations that he assessed before the application of mid-cavity forceps would balance this. It does not. The number is too small on which to build a lifetime of future obstetrics, with diminishing memory and experience, unless there is close and frequent involvement with a consultant unit. It should perhaps be added, however, that we believe that the experience gained was sufficient for the future practice of ante- and post-natal care.

PAUL O' FLANAGAN
vocational trainee

Derby

ALAN MEAKIN
vocational trainee

Children's Hospital,
Derby

1 Lloyd, G, *British Medical Journal*, 1975, 1, 79.

2 Bull, M J V, *British Medical Journal*, 1975, 3, 39.

3 Oldershaw, K L, and Brudenell, J M, *British Medical Journal*, 1975, 1, 139.

4 Elstein, M, *et al*, *British Medical Journal*, 1975, 3, 765.

5 Elstein, M, *et al*, *Journal of the Royal College of General Practitioners*, 1975, 25, 373.

6 Update, 1975, 10, 799.

Gentamicin nephrotoxicity in patients with renal allografts

SIR,—In reply to the letter from Dr J L Anderton and Dr J A Raeburn (18 October, p 165) we did not claim in our article (2 August, p 278) to have proved that gentamicin administration may cause permanent functional deterioration in renal allografts. Indeed, we stated that rejection must always be borne in mind. We did, however, provide evidence that gentamicin administration consistently causes the release of large amounts of lysosomal and other enzymes of renal tubular origin. The size of increase is greater than, and the rate of rise different from, those seen during rejection episodes. The release of enzymes is associated with changes in renal tubular cells similar to those noted in rats given gentamicin. These changes may be seen by the light microscope, as we mentioned in our article.

In rats similar changes precede those of frank tubular necrosis, although at higher gentamicin dosage. Although, as we stated, the functional changes we observed during gentamicin therapy may have been due to rejection, in the light of the other evidence of nephrotoxicity (enzymes and histology) we feel that their frequency justifies our conclusion—namely, that gentamicin should be used with caution. We did not imply that gentamicin, which we too have found useful, should not be used.

J M WELLWOOD

St Bartholomew's Hospital,
London EC1

A E THOMPSON
J R TIGHE

St Thomas's Hospital,
London SE1

Cot deaths in Sweden

SIR,—Contrast in conditions of work, play, and habitation between England and Sweden are enormous, and it is extremely difficult to draw any conclusions from comparisons between the two countries. Drs P O Petersson and G von Sydow drew attention (23 August, p 490) to the rarity of cot deaths in Sweden. As a surgeon in Sweden who has previously worked two years as a general practitioner in England I would comment that it is not unusual to see housing conditions in industrial estates in the Midlands and North of England which are almost unbelievable by Swedish standards. Cots made for one can accommodate two or even three children up to 5 years of age and beds made for two may be the abode of five and six individuals, of which the latest member of the family is usually included. Unemployment is relatively high. The bedrooms are often damp and cold, with the only heat from a gas fire. Contraception and abortion are not as readily accepted in many areas of England as in Sweden, but nevertheless a further mouth to feed is often a catastrophe.

Sweden has no equivalent of the English GP. The GP called to see a newborn baby found dead one morning may himself not only have delivered that baby but even its parents and grandparents. His prime concern therefore is to help the family rather than assist the Registrar General, which can lead to a dubious diagnosis on the death certificate to avoid endless and tiring police inquiries.

Thus the differences certainly depend on the different social and economic patterns of the two countries, of which child health care and follow-up is only a part.

DAVID FREEDMAN

Jakobsbergs Sjukhus,
Stockholm, Sweden

Cryotherapy for piles

SIR,—I was somewhat dismayed to see that Mr R E B Tagart (18 October, p 165) has condemned the treatment of piles by cryotherapy as a result of his limited experience with a liquid nitrogen probe. As far as one could gather from his letter, he had treated an undisclosed number of external piles by this method and only 10 patients with internal piles.

While I agree with him that the liquid nitrogen machine is cumbersome, a satisfactory alternative exists in the nitrous oxide cryoprobe, which is cheaper, very