ECT with curare

SIR,—In an obituary notice (9 July, p 130) in tribute to the late Dr J A Hobson it is observed that Dr Hobson "was also the first or second psychiatrist to use curare with ECT (he and Dr Aaron Gillis published papers almost simultaneously)."

In fact the paper by Hobson and Prescott¹ appeared in the same issue of the *BMJ* as did the paper by Gillis and Webster.² It should be noted, however, that Dr Hobson's technique included the now well-accepted³ use of thiopentone. The omission of thiopentone incidentally gave us the opportunity to describe² what was perhaps the first case of "awareness during operation."

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¹ Hobson, J A, and Prescott, F, *British Medical Journal*, 1947, 1, 445.

² Gillis, A, and Webster, D D, *British Medical Journal*, 1947, 1, 455.

³ Royal College of Psychiatrists, *British Journal of Psychiatry*, 1977, 131, 261.

Intrathoracic tracheal tumour presenting as asthma

SIR,—The article by Dr D Isaacs and others (19 November, p 1332) highlights a rare problem, that of differentiation of early tumour-related upper airways obstruction from simple asthma. In the patient described the opportunity for early intervention was lost when a diagnosis of asthma was made. Information obtained from measurement of maximum respiratory flow rates and flow volume curves might have been useful had some clinical suspicion or abnormality on spirometry suggested more than simple asthma, prompting further investigation. The article points out that spirometry results showing very low values for FEV₁/FVC with no symptoms at rest should alert the physician.

In addition, however, a distinction between spirometry tracings in upper and lower airways obstruction may sometimes be possible, as is mentioned in certain texts,¹ a uniformly slow expiratory flow with consequent straight-line pattern suggesting the former. Assessment by inspection of the spirometry tracing in addition to measurement of absolute values for FEV₁/FVC still has a place in respiratory investigation.

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¹ Burrows, B, Knudson, R J, and Kettel, L J, *Respiratory Insufficiency*, p 68, Chicago, Year Book Medical Publishers, 1975.

Meningeal leukaemia in lymphoid blast crisis of chronic myeloid leukaemia

SIR,—We greatly appreciated the short report of Dr R K Woodruff and others (19 November, p 1325).

Their experience is further exemplified by a 13-year-old girl who, 14 months after being diagnosed as having Philadelphia-chromosome-positive chronic myeloid leukaemia (CML), presented in acute blastic crisis. The blasts were morphologically and antigenically lymphoid. She responded to vincristine and prednisolone induction and was maintained on 6-mercaptopurine and methotrexate. But persistent severe thrombocytopenia

($<20 \times 10^9/l$ ($<20\,000/mm^3$)) for three months led to modification of chemotherapy and delay in central nervous system (CNS) prophylaxis. She relapsed after four months but was again responsive to prednisolone and vincristine. Her next relapse after a further three months was in the CNS only (vomiting, vertical headache, visual blurring, and blast count of $1.6 \times 10^9/l$ ($1600/mm^3$)) in the cerebrospinal fluid (CSF). Intrathecal methotrexate ($10\,mg/m^2$) given weekly for three doses cleared the CSF of cells, but severe thrombocytopenia ($<10 \times 10^9/l$ ($<10\,000/mm^3$)) unresponsive to platelet infusions led to a conversion to craniospinal irradiation (2400 rads in 15 fractions to the cranium plus 1000 rads in 10 fractions to the spine). Symptomatically she remained well for three more months until a further haematological relapse. At the time of writing she is again in haematological but more significantly CNS relapse.

This case underlines the severe risk of intractable meningeal and intracerebral ($\pm$ spinal) disease in acute lymphoid conversion of CML. However, the marked thrombocytopenia (presumably as a feature of stem-cell disorder) deterred us from lumbar punctures. Hypersplenism and presumed platelet antibody development negated the value of "random-donor" platelets. She also lacked a suitable "close-match" family member from whom to obtain platelets. Yet this thrombocytopenia may have been critical in the development of CNS leukaemia.¹

Craniospinal irradiation was not sufficient to deal with the problem. We would in the future look for any cells reactive to anti-acute lymphoblastic leukaemia serum at presentation of any case of CML. Their presence would indicate a need for early, full CNS prophylaxis involving intrathecal medication and irradiation plus continuing surveillance before megakaryocyte reserves have been destroyed.

We wish to acknowledge Dr George Janossy's kind help with repeated cell-typing of this patient,

O B EDEN

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¹ West, R J, et al, *British Medical Journal* 1972, 3, 311.

Hyponatraemia associated with hydrochlorothiazide treatment

SIR,—I feel it would be beneficial to publicise four cases of hyponatraemia in elderly women associated with diuretic preparations containing hydrochlorothiazide which resulted in confusional states.

Three patients aged 69, 89, and 71 who had been on long-term Moduretic therapy (one tablet a day in the first two cases and two in the morning in the third), either for hypertension or control of congestive cardiac failure, were admitted during the period June–October 1977 to this hospital with confusional states and all were shown to have low plasma sodium concentrations (112–128 mmol/l), which, after stopping the diuretic therapy, rose within a few days to normal levels. The Moduretic preparation contains 50 mg of hydrochlorothiazide per tablet. In two of these three patients there was an accompanying hypokalaemia (2.9–3.0 mmol/l).

The fourth patient, aged 81, had been on long-term Direma therapy, two tablets once a day, each tablet containing 25 mg of hydrochlorothiazide, and was admitted in an incoherent state with general weakness,

equivocal plantar responses, and generalised hyporeflexia. On admission a plasma sodium level of 114 mmol/l was found which rose within three days to 133 mmol/l after cessation of diuretic therapy. The chloride level in this patient showed an accompanying rise from an initially low level. In none of these patients was it necessary to continue with diuretic treatment.

Perhaps it is necessary to consider carefully the choice of diuretic in the older age groups owing to this risk with the thiazide-containing preparation and I would be grateful for anyone else's observations of similar instances.

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Prevention of divers' ear

SIR,—We share the view expressed in your leading article "Divers' ear" (29 October, p 1104) that what may be a mere nuisance for summer swimmers is an incapacitating illness for saturation divers. In pressure chamber experiments with warm, moist atmospheres similar to those you describe¹ we found that otitis regularly interfered with the function of the divers. Pain and other symptoms often led to the administration of sympathomimetic amines, antibiotics, and analgesics including codeine.

This letter is meant to call attention to a highly successful means of prevention.² Divers' ear can be prevented by the use of 2% acetic acid in aluminium acetate solution each morning and evening and following each wet dive. The head is tilted to one side and the canal gently filled with the solution. The solution must remain in the ear canal for five minutes. The head is then tilted to the other side to allow the solution to run out and the procedure is repeated in the other ear. The duration of the solution in the ear canal is critical to the success of the prophylaxis. The dive supervisor should observe and time ear prophylaxis when diving is taking place in waters where external otitis is known to be a problem.

This programme completely eliminated otitis externa which had occurred in 30–70% of divers. Application of other preventive efforts was ineffective. The acetic acid-aluminium acetate prophylaxis has had no adverse effects since its introduction five years ago.

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¹ Raymond, L W, *Lancet*, 1975, 1, 807.
² Thalmann, E D, *A Prophylactic Program for the Prevention of Otitis Externa in Saturation Divers*. Navy Experimental Diving Unit Report 10-74. Washington, DC, USNEDU, 1974.

HLA-B12 as a genetic marker for vesicoureteric reflux?

SIR,—Primary vesicoureteric reflux is a congenital defect due to lateral ureteric ectopia and may be inherited.¹ To date over 80 affected families have been reported,²

including at least three sets of identical twins.³ The pattern of aggregation in these families has suggested an inherited basis for a proportion of patients with vesicoureteric reflux, but no uniform pattern of inheritance has been apparent. In Christchurch we have investigated the immediate family of 42 patients with reflux nephropathy and in 12 of these families there were one or more affected members.⁴

To assess whether there may be an easily delineated genetic marker for reflux nephropathy we have looked at the tissue typing of all patients presenting recently to our department with chronic renal failure due to reflux nephropathy and compared this with the tissue types of patients with renal failure due to other causes. The results are shown in the accompanying table and indicate that HLA-B12 is occurring with significantly greater frequency in patients with reflux nephropathy.

Presence of HLA-B12 in patients according to aetiology of renal failure

Cause of renal failure	No of patients	No with HLA-B12
Reflux nephropathy	19	9
All other causes	46	8

χ^2 test with Yates's correction: $\chi^2 = 4.9$; $0.02 < P < 0.05$.

In larger centres it may be possible to confirm whether this is a valid observation and therefore possibly a genetic marker for a disease that not infrequently results in end-stage renal failure.

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¹ Bailey, R R, *Clinical Nephrology*, 1973, 1, 132.

² *British Medical Journal*, 1975, 2, 726.

³ Redman, J F, *Journal of Urology*, 1976, 116, 792.

⁴ Bailey, R R, Abbott, G D, and Little, P J, unpublished data.

Paranoid psychosis with indomethacin

SIR,—I read with interest the case report by Dr M W P Carney (15 October, p 994). I would like to report a somewhat similar case in which psychosis was thought to be related to indomethacin.

An 80-year-old woman was admitted with a two-day history of swollen and tender left lower extremities. The initial impression was that of cellulitis, for which she was treated with dicloxacillin and mini-dose heparin. The following day aspiration of joint fluid from her left knee revealed calcium pyrophosphate crystals. Indomethacin 25 mg thrice daily was prescribed for presumed pseudogout. The patient received her first dose at 2 pm. That evening at about 10 pm, she became verbally hostile, hallucinated, and paranoid, fearing that people were trying to kill her. This reaction required the administration of chlorpromazine intramuscularly, to which she responded. Since this patient had no previous history of psychiatric disturbances and was not receiving any other medications associated with such reactions the question was raised whether indomethacin could be the cause.

A literature review revealed that investigators have observed a variety of psychic disturbances.¹⁻³ The response from the manufacturer was that their files on indomethacin contain reports of psychic changes of various types. The symptomatology reported includes depersonalisation, anxiety, agitation, depression, and paranoid behaviour. These

responses have generally occurred early in therapy, most frequently after one or two doses.

While the possibility that this reaction was due to the drug was being investigated the patient received a second dose of indomethacin without complication. Subsequently, she continued to receive the drug for five days without incident.

In this case, although the time sequence and literature led one to a cause-and-effect relationship, the reaction was probably unrelated to indomethacin. Nevertheless, health care professionals should be aware that various psychic disturbances can be seen with indomethacin. These effects are generally transient and disappear when the drug is discontinued.

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¹ Katz, A M, Pearson, C M, and Kennedy, J M, *Clinical Pharmacology and Therapeutics*, 1965, 6, 25.

² Rothermich, N O, *Journal of the American Medical Association*, 1966, 195, 531.

³ Rothermich, N O, *Journal of the American Medical Association*, 1973, 226, 1471.

Syntometrine as a possible cause of neonatal jaundice

SIR,—Newborn babies often become jaundiced even when there is no prematurity or blood-group incompatibility. This so-called "physiological" jaundice has become very much commoner than it was 20 years ago and in some cases the bilirubin levels rise high enough to threaten mental impairment so that replacement transfusion has to be performed. The use of oxytocin infusions in the first stage of labour has been thought to explain some of the cases and breast-feeding has also been blamed, but these explanations are unsatisfactory.

I think the main reason may well be the almost universal use of oxytocics to expedite placental separation. If Syntometrine (synthetic oxytocin+ergometrine) is given soon after the baby's head is born the uterus usually contracts tightly while the placenta is still inside and before the umbilical cord is clamped. The placenta is squeezed like a sponge and the baby may receive a blood transfusion which it does not need. One would expect this surplus blood to be haemolysed and that could well be the source of the bilirubin which is causing anxiety to our paediatric colleagues.

We are starting an investigation here to try to prove or disprove the idea. It may have been suggested before, but if so I have not seen it. The benefits of active management of the third stage are, of course, very great and alarming postpartum haemorrhages are now quite rare, so the method is much favoured by obstetricians and midwives.

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Philadelphia-chromosome-positive childhood chronic myeloid leukaemia

SIR,—You recently published a report by Drs Angela Boque and R G Wilson of adult-type chronic myeloid leukaemia (CML) in a 5-month-old infant (26 November, p 1397). We have already reported a similar case in an 11-month-old child.¹ This case was Philadelphia-chromosome-positive and resembled the adult-type CML.

An interesting finding was that the leukaemic cells were consistently terminal deoxy-

nucleotidyl transferase (TdT) positive, a characteristic usually associated with leukaemias of T-cell origin.^{2,3} More recently we have shown that the leukaemic cells also possess high levels of N-alkaline phosphatase (N-APase) (assayed by Dr H Neumann, Weizmann Institute of Science, Israel), another "lymphoid" characteristic.^{4,5}

The child responded well to therapy and is very well and growing normally with no evidence of blastic crisis 2½ years after diagnosis. Apart from the detectable levels of the two enzymes (TdT and N-APase) the case is very similar to adult CML. Whether the presence of TdT and N-APase in this case is general for adult-type CML in such young children or is due to other factors remains to be determined.

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¹ Saffhill, R, *et al*, *British Journal of Cancer*, 1976, 33, 664.

² McCaffrey, R, *et al*, *New England Journal of Medicine*, 1975, 292, 775.

³ Hoffbrand, A V, *et al*, *Lancet*, 1977, 2, 520.

⁴ Neumann, H, *et al*, *Science*, 1974, 186, 151.

⁵ Neumann, H, *et al*, *Proceeding of the National Academy of Sciences of the USA*, 1976, 73, 1432.

Bell's palsy and herpes simplex

SIR,—Although increasingly, as I get older, I am prepared to believe that magic has a place in the practice of medicine, its value in clinical virology must still be limited. Dr P Grout's letter (3 December, p 1480) does not provide any evidence that his case of Bell's palsy was caused by herpes simplex. The lack of "numerical information" is indeed very important. The antibody titres (it is not stated whether they are neutralising or complement-fixing antibody titres) to herpes simplex virus (HSV) and varicella zoster (VZ) are both given as ≥ 1280 . Although my experience of zoster of necessity is limited (I have not yet seen my five thousandth case), it is not true that seventh nerve palsy is uncommon in zoster. About 2% of the many patients referred to me each year with zoster have facial zoster. A complement-fixing titre of ≥ 1280 is suggestive of recent infection with VZ virus. Unless the patient had chickenpox, and I assume it is unlikely that the lesions were confined to the mouth, the patient must have had zoster. Occam's razor usually only has one edge in this country and it is not unreasonable to assume that the patient had motor zoster of the seventh nerve. Herpes simplex infection may precipitate zoster, as may any other febrile illness. It is possible that Dr Grout's patient had primary herpetic gingivostomatitis. One cannot make a firm diagnosis without viral cultures. I agree that recurrent herpetic gingivostomatitis is uncommon, but this makes it so much more important that paired sera should have been taken because we do not know whether the episode was one of a primary infection.

I submit, then, that Dr Grout's case is not proved.

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