

who had had two short episodes of jaundice as a child. Anaesthesia for his operation for varicose veins was induced with thiopentone and continued with nitrous oxide, oxygen, and halothane in a semi-closed circuit. Urine analysis on the day of operation was normal but after the operation the patient was noticed to be jaundiced. Liver function tests showed an increase in the conjugated serum bilirubin to 3.8 mg/100 ml and in the total serum bilirubin to 4.5 mg/100 ml. Concentrations of aspartate transaminase and alanine transaminase were within normal limits. Urine analysis was positive for bilirubin, urobilinogen, urobilin, and bile acids.

The jaundice decreased, but 15 days after the operation both the conjugated and total serum bilirubin were still raised. The only abnormal finding in the urine now was a positive test for urobilin. Five days after the operation the possibility that the jaundice was due to halothane was investigated, but a normal SGPT and SGOT, a normal alkaline phosphatase, absence of eosinophilia, and no undue pyrexia made a diagnosis of halothane hepatitis improbable. It was thought that the patient possibly had the Dubin-Johnson syndrome.

He had meanwhile been discharged after a normal convalescence and had remained in excellent health. Three months later a further bromsulphalein test showed 63% dye retention in 5 minutes, 20% dye retention at 25 minutes, and 18% dye retention at 45 minutes. The second and third percentages, indicating difficulty in excretion of the dye, are consistent with the diagnosis of the Dubin-Johnson syndrome and probably the jaundice was due to that and not to the anaesthetic.—I am, etc.,

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¹ Robbins, S. L., *Pathology*, 3rd edn., p. 185. Philadelphia, Saunders, 1967.

Halothane, Hepatitis, and Dental Anaesthesia

SIR,—While the precise relationship, if any, between halothane and hepatitis remains unsolved, it nevertheless appears likely that it is in the field of multiple administration that the most fruitful observations may be made. There is one branch of anaesthesia which does not appear to have attracted attention in this context, possibly because the multiple sequence is not often encountered in hospital practice. I refer to general anaesthesia for dentistry.

There are two types of dental case which are subjected to more than one anaesthetic within a short space of time: serial extractions for orthodontic purposes, and multiple extractions or "clearance" prior to dentures.

It is the second group which is of interest, for not only is the age group within the susceptible range, but the patients would be remarkably free from extraneous influences such as hospitalization, drug therapy, injections, investigations, transfusions, etc. The usual pattern is that the posterior teeth on one side are extracted at the first session; one or two weeks later the contralateral posterior teeth are extracted; some three months later the anterior teeth are extracted for immediate denture replacement.

It is not possible to say how frequently halothane is administered in this pattern, but certainly the drug has been widely used in

this type of dental anaesthesia for many years. Since there are some 1,250,000 dental anaesthetics administered annually in N.H.S. surgeries, the number of cases which have been "at risk" might be very large indeed. While obscure pyrexia or even transient jaundice following the first administration might well have escaped notice or comment, it seems unlikely that massive hepatic necrosis following closely on the second administration would have for so long remained unrecorded.

I should be interested to hear of examples of jaundice following a dental anaesthetic of any type.—I am, etc.,

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Amphetamine Prescribing in Bristol

SIR,—In 1968 a B.M.A. committee recommended a drastic reduction in stores held and prescriptions of amphetamine-containing drugs.¹ In December 1969 the Ipswich Local Medical Committee obtained the unanimous agreement of members to cease prescribing these drugs and this was effective,² the chemists being able to dispose of stocks and the police noting a dramatic fall in amphetamine abuse.

In 1970 the Bristol Local Medical Committee asked all practitioners to drastically reduce and if possible abandon completely preparations containing amphetamines.

In August 1971 I asked all chemists on the Bristol Executive Council list to record the number of prescriptions and quantity of drug issued for 31 amphetamine-containing preparations during September and October. I asked them not to record the name of the doctor or patient concerned. Out of 108 chemists 63 (58%) sent complete replies and several returned incomplete forms.

| | No. Prescriptions | No. Tablets | Mg Amphetamine |
|----------|-------------------|-------------|----------------|
| Per Week | 84 | 4,531 | 34,070 |
| Per Year | 4,391 | 235,600 | 1,719,000 |

The Table gives figures based on the assumptions that for present purposes the 45 chemists not given adequate data handled the same quantities as those that did and that prescribing rates are similar throughout the year.

A quarter of a million tablets, allowing for their use in narcolepsy and hyperkinesia, is a lot, even for a population of half a million.

Dexedrine, dexamphetamine, Drinamyl, and Durophet were still prescribed in large quantities, though many chemists commented that there had been a fall in amphetamines prescribed in the previous two years. There is no accurate record of the quantities prescribed before, but it does seem that while the quantity has fallen it might be time for a further attempt to discourage most strongly the use of amphetamines both in Bristol and probably throughout the country.

I am very grateful for the help of the secretaries of the Bristol Executive Council, Local Medical Committee, and Local Pharmaceutical Committee.

—I am, etc.,

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¹ *British Medical Journal*, 1968, 4, 572.
² Wells, F. O., *British Medical Journal*, 1970, 2, 361.

Respiratory Depression in Tricyclic Overdose

SIR,—The pattern of tricyclic antidepressant overdose is now well recognized (2 January 1971, p. 3). Complications include convulsions,¹ arrhythmias, and E.C.G. changes.² However, respiratory depression does not generally occur. Doxepin (Sinequan) is a new tricyclic antidepressant and few reports of overdose have been described. Approximately 800 mg caused epileptic fits for 24 hours in a patient who recovered uneventfully; 600 mg taken by another patient resulted in drowsiness for 24 hours. The case report below illustrates that severe respiratory depression may occur in doxepin overdose.

A woman of 54 took 1,500 mg (60 capsules) of doxepin in a suicidal attempt. Within one hour she was having generalized convulsions, and was deeply unconscious. She was cyanosed with extremely poor respiratory effort. No reflexes could be elicited and her pupils were dilated and unreactive. Blood pressure was 65/30, pulse feeble and rapid, and E.C.G. showed a ventricular tachycardia, the rate varying between 60 and 150 per minute.

Assisted respiration produced a dramatic improvement in her cardiovascular state, the E.C.G. returning to normal within an hour. However, respiration remained severely depressed and she needed ventilation for 16 hours altogether. Within 24 hours the endotracheal tube was removed and she subsequently made a good recovery.

The recommended dose of doxepin is 30-300 mg daily in divided doses. The patient reported above took 1,500 mg, only five times the maximum daily dose, but this was sufficient to cause potentially lethal respiratory depression. As another patient has had fits with 800 mg it would seem that where there is a serious risk of suicide no more than 500 mg (twenty 25-mg capsules) should be prescribed at one time.

I am grateful to Dr W. R. N. Friel, Dr. S. Ruttle (Committee on Safety of Drugs), and Pfizer Ltd. for the information which they provided.

—I am, etc.,

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¹ Steel, C. M., O'Duffy, J., and Brown, S. S., *British Medical Journal*, 1967, 3, 663.

² Barnes, R. J., Kong, S. M., and Wu, R. W. Y., *British Medical Journal*, 1968, 3, 222.

Pollution and Population

SIR,—The recent correspondence on pollution and population has aroused considerable interest among several of my colleagues.

The International Federation of Medical Student Associations is planning a symposium on pollution and overpopulation, to take place in Edinburgh on 20, 21, and 22 April before an audience of medical students from medical schools all over the world, and it is hoped, members of the British medical profession. H.R.H. Prince Philip, Duke of Edinburgh is among the patrons of this symposium, and more than 20 speakers of international repute are to participate.

This event is designed to examine in depth the practical means available for dealing with these two great threats to the environment. Perhaps its greatest achieve-