dipped into the urine. When 5 ml. of this was applied to a 3-in.×3-in. (7.5-cm.×7.5-cm.) doubled piece of towel, a much reduced colour was observed on testing, and after an hour several skilled observers recorded a negative or doubtful reaction. The cellulose napkin, when used in the same manner, gave a definite positive even after two hours. These findings were consistent on four separate occasions. Quantitative estimation suggested some instability on the towel napkins associated with urine of high *p*H, but results varied and difficulty with turbidity from traces of detergent left from washing were experienced. However, it was found that the quantity of urine taken up by a Phenistix was much less from towel-type napkins than from cellulose or by direct dipping, as shown by the increase in weight. Average of 10 tests: dipping 29.4 mg., cellulose 39.5 mg., and towel 16.5 mg.

We suggest that this reduced uptake may be responsible for a lowering of sensitivity when Phenistix is used to detect phenylpyruvic acid on towelling napkins, especially when the urine has been given time to spread over a larger area from the original point of application. Perhaps the use of cellulose napkins would increase the detection rate of phenylketonuria to an acceptable level, as they appear to provide a more favourable material for an adequate transfer of urine to Phenistix.—We are, etc.,

D. A. BAXTER.
M. E. YORK-MOORE.

Royal Eastern Counties Hospital,
Colchester, Essex.

Mercury Perchloride in Surgery

SIR,—We were interested in the letter by Mr. D. H. Patey (28 October, p. 238) suggesting that an accurate evaluation be made of the use of mercury perchloride in eradicating malignant cells from operation wounds. Like Mr. Patey, we too had not found any evidence of this having been done, and began some experiments some nine months ago. It is too early yet to make a complete evaluation, but our preliminary results using T_{241} sarcoma cells in C_{57} mice are encouraging and are summarized below.

Wounds Seeded with Sarcoma Cells

Irrigating Solution	Saline	Hypochlorite	0·1% Mercury Perchloride
Number of mice used	98	82	47
Number of mice in which tumours grew	88	40	11
Percentage in which tumours grew ..	90	49	23

In our earlier experiments[1,2] we found that, using carcinoma cells under similar experimental conditions, cetrimide solution was more effective than other agents tested in preventing growth of malignant cells in operation wounds. The other agents tested included nitrogen mustard solution and hypochlorite solution.

In view of the favourable early results using mercury perchloride, we are currently comparing the effects of mercury perchloride solution with other irrigating solutions, including 1% cetrimide solution, in experimental wounds seeded with carcinoma, sarcoma, and melanoma cells.—We are, etc.,

GEOFFREY R. GIBSON.
FREDERICK O. STEPHENS.

Department of Surgery,
University of Sydney,
Sydney, Australia.

REFERENCES

1 Stephens, F. O., and Gibson, G. R., *Cancer (Philad.)*, 1966, 19, 1286.
2 Gibson, G. R., and Stephens, F. O., *Lancet*, 1966, 2, 678.

Oculogyric Crisis after Phenothiazines

SIR,—A nurse, aged 21, was recently admitted to this hospital with a severe oculogyric crisis following an injection of Fentazin (perphenazine) 10 mg. given for unexplained vomiting. She also complained of a choking sensation, had severe trismus, and presented a dramatic clinical picture.

In view of the fact that this appeared to be an extrapyramidal syndrome, as described in the manufacturer's literature, she was given atropine (0.6 mg.) as a potent anti-Parkinsonian drug. Pethidine (50 mg.) was also given. This was followed by a complete remission of symptoms within 10 minutes. There was a minor recurrence two hours later and she was given a second dose of atropine (0.6 mg.). After this she had no further symptoms.

Although this complication of Fentazin therapy is mentioned in the manufacturer's literature there is no reference to treatment.

This particular patient gave a history four months before of taking perphenazine tab. 4 mg. b.d. for five days without any adverse effect. This raises the possibility that the patient had been sensitized by the earlier administration of the drug, but such sensitization does not appear to have been previously described.—We are, etc.,

J. J. KIMERLING.
S. R. PATEL.

Heatherwood Hospital,
Ascot, Berks.

Safety of Dimethoate Insecticide

SIR,—The organophosphate anticholinesterase insecticide dimethoate is widely used in many countries for the systemic control of insects on food crops. At harvest some recently treated crops contain a small residue of dimethoate, from 0.05 up to 1 p.p.m. The safety of such residues to consumers of the crops is clearly an important matter.

Toxicological studies conducted before marketing showed that dimethoate intake rates as high as 0.04 mg./kg. bodyweight per day produced no detectable effect on whole-blood cholinesterase (ChE) values in rats (trial duration 6–12 months) or in human volunteers (duration one month). Individual human subjects were also given 0.13 and 0.26 mg./kg./day respectively for 21 days without detectable effect.[1] A special F.A.O./W.H.O. committee responsible for reviewing safe levels of pesticides in food was naturally reluctant to accept data on individual subjects, and recommended the maximum allowable intake rate for dimethoate as 0.004 mg./kg./day.[2] This is the intake rate shown harmless to humans but reduced by a safety factor of 10. This recommendation tended to limit the permissible uses of an efficient insecticide with an excellent record of safe use in the field. Further studies were therefore desirable.

We now report extended observations on the response of humans to the daily ingestion of dimethoate, and in particular on the daily intake rate required to cause depression of whole-blood ChE values.

Thirty-six male and female adult volunteers without occupational exposure to organophosphate insecticides were arranged in groups and given repeated doses of dimethoate as indicated in the Table. Actual dosage was on five days per week, and each daily dose was therefore seven-fifths that shown in the Table. Missed doses of one or two days were made up by double doses on the day before or after. The dimethoate was administered as a flavoured aqueous solution. Venous blood samples were taken twice before and once or twice per week after dimethoate dosage started. ChE in whole blood was measured by the electrometric method of Michel[3] and its depression taken as the critical first response to dimethoate. Activity in red cells and plasma were also determined separately. The study was under close medical supervision, and inquiry was also made for any effects other than ChE depression, though none was detected.

The Table summarizes the experimental plan and results of the study. ChE values are expressed in "cholinesterase units" (ΔpH/hr.×100). Groups D and E were made up of previously discontinued Groups A and B, and were included to confirm at higher dosage levels the response seen in Group C.

The results show that no significant change occurred in Groups A and B. ChE values in Group C began to show a slow downward trend by day 20, and this continued to the end of the test at 57 days. Groups D and E showed the same effects at an earlier stage, and a somewhat faster rate. The rate and extent of red cell ChE depressions closely paralleled those of whole-blood ChE in Groups C and D. No localized gastrointestinal or other clinical effects occurred in any group.

From this study we concluded that dimethoate ingestion by humans at the rate of 0.4 mg./kg./day or above will cause a slow decrease in whole-blood ChE activity, but that at 0.2 mg./kg./day and below such an effect is most unlikely to occur. (Eight subjects were studied at a mean intake rate of 0.2 mg./kg./day. Their range of ChE activity before ingestion was 108–148 units (mean±2 standard deviations) and after 39 days was 102–146 units.)

It is therefore suggested that the experimentally adduced "no-effect level" for dimethoate ingestion by small groups of humans may now safely be taken as 0.2 mg./kg./day, which when reduced by a safety factor of 10 would imply an acceptable daily intake rate

Group	No. in Group	Daily Dose mg. Dimethoate	Duration of Test (days)	Mean Whole Blood ChE		Mean Weight (kg.)	Daily Intake Rate (mg./kg./day)
				Before	At End		
A	12	5	28	114	110	74	0·068
B	9	15	39	128	124	75	0·202
C	8	30	57	121	92	71	0·434
D	6	45	45	113	74	77	0·587
E	6	60	14	121	96	60	1·02

of 0.02 mg./kg./day. This is equivalent to the daily consumption by 60-kg. humans of 1 kg. of foodstuff containing 1.2 p.p.m. dimethoate residue. It bears a safety factor of at least 10 before the slightest effect on blood ChE activity would occur, and (from animal studies) a safety factor of about 400 before the first signs of clinical toxicity would arise. The full details of this study will be reported elsewhere. It is hoped that the findings may extend the permissible usage of an important and safe insecticide.

Grateful acknowledgement is made to the 36 volunteers concerned and to Soc. Montecatini (Milan) for providing the necessary materials.

—We are, etc.,

E. F. EDSON.
K. H. JONES.
W. A. WATSON.

Chesterford Park Research Station (Research Centre of Fisons Pest Control Ltd.), Saffron Walden, Essex.

REFERENCES

1 Sanderson, D. M., and Edson, E. F., *Brit. J. industr. Med.*, 1964, 21, 52.
2 F.A.O./W.H.O. Joint Report, 1965, *Evaluation of the Toxicity of Pesticide Residue in Food.* Rome.
3 Aldridge, W. N., and Davies, D. R., *Brit. med. J.*, 1952, 1, 945.

Injury from High-speed Drills

SIR,—A serious ophthalmological hazard exists to dental practitioners from the new high-speed drills used for cavity preparation in teeth. Particles of filling or other dental debris may be projected at great speed into the orbital region of the operator, and cause damage to the eye.

In a recent case a fragment of tooth substance, propelled in this way, caused a severe corneal abrasion, which prevented the dental surgeon from working for a considerable period of time.

The necessity to wear some form of eye protection, such as goggles or spectacles, while using these drills cannot be too strongly stressed.—I am, etc.,

N. E. A. RENNER.

Eastman Dental Hospital, London W.C.1.

Psychotropic Drugs

SIR,—As the co-author of the first British paper on phenelzine[1] I should like to comment on the views of Dr. P. Leyburn and his colleagues (18 November, p. 417).

In designing that first trial I was deeply concerned about the dangers of prescribing a placebo for depressed patients, since suicide is a possible outcome of imperfectly treated depressed patients. That risk was taken in the trial described but was not taken in any subsequent trial. The M.R.C. trial[2] expected a large number of investigators to take a similar risk, and this is one reason why I did not take part in the M.R.C. trial. In the design of any further trial one would hope that the M.R.C. would take the advice of people like Dr. P. J. Dally (28 October, p. 233) who are engaged in active clinical psychiatry. The previous trial was concerned with a type of patient who is found only in the pages of the older history books on psychiatry.

One of the hidden advances that monoamine oxidase inhibitor drugs and tricyclic compounds have given us has been the discovery of hitherto unsuspected varieties of depression. The important task now is to marry symptomatology up with treatment. No single antidepressant drug is a specific cure for all varieties of depression.

It is time that clinicians ceased to be afraid of the dangers of these drugs. I have not seen one death from them in eight years of use, but I have seen several deaths from suicide in that period. Yet the deaths from suicide appear to be fewer than they were before these treatments were available. It would be of value for investigators to use the suicide rate as an index of success or failure in treatment.

In conclusion, it is important to remember that the elimination of suicide in depression is the main goal of all types of treatment. The suicide rate is still comparable to the death rate from road accidents, but the research and publicity directed towards its elimination compare very unfavourably with the efforts of the Ministry of Transport in dealing with its particular problem.—I am, etc.,

Cane Hill Hospital, Coulsdon, Surrey. JOHN T. HUTCHINSON.

REFERENCES

1 Hutchinson, J. T., and Smedberg, D., *J. ment. Sci.*, 1960, 106, 704.
2 Report to the M.R.C. on Treatment of Depressive Illness, *Brit. med. J.*, 1965, 1, 881.

Surgery in Pulmonary Tuberculosis

SIR,—Your leading article "Surgery in Pulmonary Tuberculosis" (21 October, p. 127) defined six groups of patients who still require surgical treatment to complete their recovery. The fourth group contained "a few patients with 'healed cavities' which have become secondarily infected with aspergillus fungus. . . ."

The British Tuberculosis Association (B.T.A.) investigation, to be published shortly, into the incidence of aspergillus infection in "open healed" cavities has shown that the incidence is not negligible. In my own clinic, with approximately 1,000 patients on the tuberculosis register, we have 19 patients with "open healed" cavities, and no fewer than eight of these show evidence of aspergillus infection, six have a classical mycetoma demonstrated radiologically and have positive precipitin tests, and two have positive precipitin tests but so far no radiologically demonstrable mycetoma.

Resection in the presence of aspergillus infection is a more difficult and dangerous operation than resection in the absence of infection, and I submit that the likelihood of a young person left with such a cavity developing mycetoma in the future is sufficiently high to warrant resection of such residual cavities after adequate antituberculous chemotherapy, usually of two years' duration.—I am, etc.,

T. A. W. EDWARDS.

Chest Clinic, St. Albans City Hospital, St. Albans, Herts.

In Advance

SIR,—The correspondence on obstetric forceps or vacuum extractor (4 November, p. 292, and 11 November, p. 354) and on institutional care of the mentally subnormal (11 November, p. 355) reminds me of the saying, "What Manchester thinks today London thinks tomorrow."

In the former, "the fact that it (the vacuum extractor) has largely replaced the forceps in several countries on the Continent" applies also to Northern Ireland and probably to other regions of the British Isles outside London.

In the latter, Northern Ireland for 10 years or more has cared for the mentally subnormal in the community with schools, and more recently with sheltered workshops and hostels.

Last month a swimming-pool exclusively for the use of the mentally subnormal was opened by Lady Wakehurst at Muckamore Abbey. Before this, hydrotherapy had been given at public swimming-baths, a treatment for the mentally subnormal which has been pioneered in Europe by Northern Ireland.

Several other advances in medical science have been instigated for the first time in the British Isles in Northern Ireland which I am reluctant to list for fear of appearing to boast. But the matters raised might indicate to your readers that here we appear to be in advance of, not behind, the times, and that the days of "pigs in the kitchen" have long passed away if they ever did exist.—I am, etc.,

Belfast 9. MARY N. M. PAULIN.

North America Interview Board

SIR,—I would be grateful to be allowed to reply to the letters of Dr. J. Stanners and of Dr. C. D. H. Elton and Mr. I. W. M. Wright (18 November, p. 416).

The Interview Board's tour was arranged to meet the requests for interviews received in answer to the Ministry's advertisement of our visit published in the *B.M.J.* and other journals in July and August. Such requests were still reaching me when the Board left England on 30 September. At this time we had already invited 150 doctors to meet us for discussions of up to one hour each. It was possible to make only a few adjustments to this programme, because it was already very full and because the team's travelling schedule had to be adhered to. Every effort was made to accommodate doctors who approached the team at short notice, and where this was not possible informal meetings with individual members of the Board were arranged. I am sorry if some British doctors in Alberta were unaware of our visit before receiving a letter from the British Head of Post in Edmonton, but this, as I have said, was not the first intimation of our visit.

The Board would have gladly visited Edmonton if a sufficient number of doctors there had asked to meet us, but the centres chosen were necessarily locations which suited the convenience of the majority of doctors who had replied to the Board's advertisements. We sincerely regret that some of the doctors who approached us at very short notice could not be seen; this happened only where the Board's time was entirely taken up with appointments already arranged and confirmed.—I am, etc.,

R. H. BARRETT,
Chairman,
Interview Board, Ministry of Health.
London S.E.1.