occurred in only 6 of the 150 cases (4%) and then only in those who received a relatively large volume of the suspension. The drug was completely non-toxic when given in tablet form.

This drug represents a great improvement on the previously used oxyuricides and can be hailed as a milestone in the treatment of oxyuriasis.

I wish to thank Dr. Mousik, superintendent, St. George's Hospital, Bombay, for allowing me to undertake this study on hospital patients. Thanks are also due to Dr. Nazareth, paediatrician, St. George's Hospital, for allowing me to use his paediatric cases for this study. Finally, thanks are due to Parke, Davis and Company, Detroit, for supplying "vanquin" free of cost.

REFERENCES

- Beck, J. W., Saavedra, D., Antell, G. J., and Tejeiro, B. (1959). *Amer. J. trop. Med. Hyg.*, **8**, 349.
 Bumbalo, T. S., Plummer, L. J., and Warner, J. R. (1958). *Ibid.*, **7**, 212.
 — (1960). *Amer. J. Dis. Child.*, **99**, 617.
 Miller, J. H., Anthony, S. O., Swartzwelder, J. C., Frye, W. W., and Lampert, R. (1958). *Amer. J. digest. Dis.*, **3**, 229.
 Royer, A. (1956). *Canad. med. Ass. J.*, **74**, 297.
 — and Berdnikoff, K. (1962). *Ibid.*, **86**, 60.
 Weston, J. K., Thompson, P. E., Reinertson, J. W., Fiske, R. A., and Reutner, T. F. (1953). *J. Pharmacol. exp. Ther.*, **107**, 315.

Medical Memoranda

Hypoglycaemic Coma During Change from Insulin to Tolbutamide

Since the introduction of tolbutamide as an oral hypoglycaemic agent in 1955, increasing numbers of diabetics have been successfully treated with this drug.

The change from insulin to tolbutamide in a suitable case is usually uneventful, and there may be a temptation to try this without first admitting the patient to hospital. It is not generally recognized that hypoglycaemic coma can occur during the change-over; the rapidity of onset and severity of such a coma is shown in the following case.

CASE REPORT

A 67-year-old woman who was first found to have diabetes at the age of 42 was admitted to hospital on December 24, 1961, because of increasing breathlessness and swelling of the legs and abdomen of six months' duration. For three months she had been having angina of effort, severe orthopnoea, and paroxysms of nocturnal dyspnoea. She also complained of dizziness and confusion and there was difficulty in giving her insulin. Since 1950 she had been stable on a diet of 10 black and 10 red Lawrence lines and 20 units of insulin zinc suspension daily.

On examination her weight was 15 st. 10½ lb. (100 kg.). The cranial nerves were intact. The fundi showed many hard exudates and haemorrhages, and arteriovenous nipping. The heart was enlarged to the left, the sounds were normal, and the blood-pressure was 180/110. The jugular venous pressure was not raised. There was pitting oedema of the legs extending to the mid-thigh. Initial serum electrolytes were normal and the blood urea was 74 mg./100 ml. The urine contained albumin and a few pus cells, but was sterile. The E.S.R. was 30 mm. in the first hour (Westergren). Serum protein estimations showed a total protein of 4.7 g./100 ml. (albumin 2.6 g., globulin 2.0 g.) (Biuret method), and there was an increase in the alpha₂-globulin fraction. Zinc sulphate turbidity was 2 units. There was 5 g. of protein per litre of urine (Esbach method).

She was well stabilized and aketotic on 10 black and 10 red lines and 20 units of insulin zinc suspension daily; however, she continued to have albuminuria averaging 9 g./l. each day. On January 16, 1962, the serum albumin had fallen to 1.2 g., the serum globulin was 2.8 g./100 ml., and the blood urea was 76 mg./100 ml.

In an attempt both to raise the serum albumin (Fister and Benas, 1960; Singh *et al.*, 1961) and to avoid the anticipated difficulties of insulin administration on discharge, it was decided that tolbutamide should be substituted for insulin. The insulin zinc suspension was stopped on January 17 after a dose of 20 units at 7 a.m. At 8 a.m. the following day she was given 1 g. of tolbutamide, and this was repeated at 2 p.m. At 4.45 p.m., after tea at 3.45 p.m., she was noted to be comatose and sweating profusely. She was promptly given 60 ml. of 40% glucose intravenously and recovered rapidly. Tolbutamide was withheld that evening and the urine was sugar-free during the night and next morning. She was rational and ate her meals normally. At 8 a.m. on January 19, 1 g. of tolbutamide was given, and at 5 p.m. the same day she again became hypoglycaemic, the blood sugar being 40 mg./100 ml. Further intravenous glucose was given and she recovered. She was restabilized on 20 units of insulin zinc suspension daily, but on January 21 had a myocardial infarct and died. Permission for necropsy was refused.

DISCUSSION

Mild hypoglycaemic symptoms are quite common in patients established on tolbutamide. In one large series symptoms attributable to hypoglycaemia were found in 6% of cases treated (Stowers and Bewsher, 1962). "One or two deaths have occurred in old people apparently from hypoglycaemia" (*B.M.J.*, 1957), but there are few reports of hypoglycaemic coma occurring (Schwartz, 1961). However, McKendry (1957) described a fatal case of hypoglycaemia in an elderly arteriosclerotic malnourished woman who had previously been hypoglycaemic on insulin; he cautioned against the use of tolbutamide in these circumstances. Severe and prolonged hypoglycaemic coma has been reported in the treatment of Parkinsonism with tolbutamide (Yonet and Ballard, 1961). Cosnett (1961) described irreversible cerebral damage following tolbutamide "overdosage."

One can speculate that in certain patients there is a sensitivity to tolbutamide and an overreaction of the remaining islet cells and subsequent severe and dangerous hypoglycaemia. We feel that under these circumstances the introduction of tolbutamide, particularly after insulin therapy, should be done only under hospital conditions. The correction of any untoward hypoglycaemia can be prompt and life-saving under such conditions. Little recognition of this complication of tolbutamide therapy has been given in the British literature, and the makers of tolbutamide have not mentioned this as a complication in their recent publications.

I. McLEAN BAIRD, M.D., M.R.C.P.
 D. F. RICKARDS, M.B., Ch.B.

Medical Unit,
 St. Helen's Hospital, Barnsley.

REFERENCES

- Brit. med. J.*, 1957, **2**, 344.
 Cosnett, J. E. (1961). *S. Afr. med. J.*, **35**, 43.
 Fister, V., and Benas, A. (1960). *J. Endocr.*, **20**, 320.
 McKendry, J. B. R. (1957). *Canad. med. Ass. J.*, **76**, 572.
 Schwartz, J. F. (1961). *J. Amer. med. Ass.*, **176**, 106.
 Singh, I., Sehra, K. B., and Bhargava, S. P. (1961). *Lancet*, **1**, 1144.
 Stowers, J. M., and Bewsher, P. D. (1962). *Ibid.*, **1**, 122.
 Yonet, H. M., and Ballard, H. S. (1961). *N.Y. St. J. Med.*, **61**, 1939.