THIOPENTONE IN ADDISON’S DISEASE

By JOHN W. DUNDEE

Operations are very rarely carried out in subjects with Addison’s disease. The reason for this is well expressed by Rowntree and Snell (1931) viz. “If treatment necessitates any surgical procedure, the risk is prohibitive and should be assumed only after most serious consideration.” It is easy to understand why anaesthesia for these subjects receives no mention in the literature. Lundy’s (1942) choice of agent would be di-vinyl ether, but he does not mention having anaesthetized any cases. Simpson (1950a) recommends local analgesia for D.O.C.A. implants but does not give any reasons for his dislike of general anaesthesia in this condition.

Examination of particulars of 14 reported operations in subjects with Addison’s disease (Rowntree and Snell, 1931; Katz and Mainzer, 1941; Leavitt, 1945; Simpson, 1950b) reveals that a severe crisis followed operation in 11 instances. With two exceptions the crisis proved fatal. Sufficient details are not available to incriminate the anaesthetic agent as a cause of the Addisonian crisis in any of these cases. The relationship between the anaesthetic agent and the Addisonian crisis is clear in the following case.

CASE REPORT

July 4, 1950. A woman, aged 45 years, weighing 9 stones (57 kg.) was admitted to hospital in Addisonian crisis. She was vomiting persistently, B.P. was 96/60, blood sugar 45 mg. per cent and blood urea 75 mg. per cent. Treatment with Eschatin, D.O.C.A. and intravenous drip of 5 per cent dextrose in normal
saline did not produce a satisfactory response and 48 hours after admission B.P. was 80/50. Failure of response to treatment was attributed to urinary infection and when this was eliminated her condition improved immensely.

August 9, 1950. Clinical improvement was sustained; B.P. given as premedication prior to D.O.C.A. implants, which it was 110/70; Hb 75 per cent; R.B.C.s 3.5 million per cu. mm.

August 14, 1950. B.P. 100/65. Morphia gr. ½ (10 mg.) was intended to insert under local analgesia. Owing to a misunderstanding 0.4 g. thiopentone was administered. This was not followed by any undue respiratory depression, but the following sequence of events ensued:

5 minutes B.P. 50/30, oxygen administered.
25 minutes B.P. 50/30, implant carried out without any response from the patient.
1 hour B.P. 60/30.
1½ hours B.P. 60/30, reacted to supraorbital pressure.
2½ hours B.P. 65/30, regained consciousness.
3 hours B.P. 70/40, very drowsy, 5 ml. Eschatin intramuscularly.
6 hours B.P. 70/50, still drowsy, 5 ml. Eschatin intramuscularly.
12 hours B.P. 70/50, still drowsy, intravenous drip of 5 per cent dextrose in normal saline commenced.
18 hours B.P. 85/50, one litre of infusion given, blood sugar 75 mg. per cent.

Mild crisis continued for further 24 hours, followed by complete recovery.

February 8, 1951. Further implants of D.O.C.A. carried out under 1 per cent procaine analgesia. There was an uneventful convalescence with no Addisonian crisis.

COMMENT

There seems little doubt that the rapid deterioration in the patient’s condition was due to the thiopentone, as the collapse occurred before the operation commenced. This view is substantiated by the uneventful convalescence on the second occasion, when no thiopentone was given. The narcosis was prolonged, as the subject did not react when the skin was incised 25 minutes after 0.4 g. thiopentone, did not regain consciousness for 2½ hours, and remained drowsy for a further 10 hours.
A fall in blood-pressure of the severity and duration recorded above is abnormal as, in the absence of operative shock or blood loss, blood-pressure returns to normal 10–15 minutes after the injection of thiopentone (Lockett, 1951). Blood-pressure in subjects with Addison’s disease is very labile and possibly unduly sensitive to the action of depressant drugs. It has been noted that more extreme falls in blood-pressure are seen following the use of thiopentone in subjects already suffering from hypotension (Adams, 1944).

The rapid recovery that follows small doses of thiopentone is due to rapid diffusion of the drug to body tissues (Mark et al., 1949; Brooks et al., 1948) and fat (Mark et al., 1950). This diffusion would be interfered with by hypotension. In the crises of Addison’s disease there is retention of potassium and excessive excretion of sodium chloride, causing dehydration of intracellular tissues. Extracellular dehydration would further interfere with diffusion of thiopentone. Both these factors would result in prolongation of thiopentone narcosis.

The adrenalectomized animal, or the patient with Addison’s disease, manifests a tendency to hypoglycaemia, more marked under conditions of fasting or stress (Simpson, 1950b). A drop of blood-pressure to 50/30 must be considered sufficient stress to bring on hypoglycaemia. The blood sugar of this subject 18 hours after the thiopentone was 75 mg. per cent. Since one litre of 5 per cent dextrose (50 g. glucose) had been given immediately before this estimation, it is very likely that hypoglycaemia played a part in prolongation of the thiopentone narcosis. Coma in Addison’s disease is most commonly due to hypoglycaemia.
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The possibility exists that hypoglycaemic coma followed the thiopentone, giving the impression that the action of thiopentone was prolonged.

Prolonged hypotension, persistent vomiting and inadequate food intake could cause hepatic dysfunction (Davison et al., 1946) and increase the duration of thiopentone (Shideman et al., 1949). Flocculation tests, hippuric acid excretion and urinary urobilinogen in this subject were all within the limits of normality and preclude any severe liver dysfunction. Oliguria and raised blood urea are features of Addisonian crises, such as occurred following the thiopentone. Although blood urea was not estimated in this subject, it is unlikely that the urea could have risen to an extent capable of potentiating thiopentone (Richards, 1950) in the short time before the subject gained consciousness.

SUMMARY

The administration of thiopentone to a subject with Addison’s disease was followed by severe hypotension and a crisis lasting for 48 hours. The various factors that could have played a part in this sequence of events are discussed. Hypotension, electrolyte imbalance and hypoglycaemia are most likely to have engendered in this subject sensitivity to thiopentone.

I am indebted to Dr. W. Sutton for permission to publish this case.

REFERENCES

Dr. Gillespie writes:

On 15th June, at a Convocation of the University of Wisconsin, the Honorary Degree of Doctor of Science was conferred on Dr. Ralph M. Waters. In presenting the candidate Professor Weaver recalled the bon mot of Dr. C. R. Bardeen, then Dean of the Medical School. When Dr. Waters first came to Wisconsin, Dr. Bardeen introduced him to the faculty with the remark that it was a unique distinction to have been appointed for his ability to put people to sleep. Dr. Waters soon showed, the speaker continued, that he was equally competent at waking people up! Professor Weaver then gave an epitome of Dr. Waters’ work, quoting extensively from a biography which had appeared in this Journal. President E. B. Fred, in conferring the degree, said that he did so gratefully and with deep affection, “because your work has focused the attention of the world on this University.”