AN INVESTIGATION OF THE PROPERTIES OF ISOPROPYL CHLORIDE

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MacDonald (1950) has described the anaesthetic properties of isopropyl chloride ("proponesin"). This agent has now been used by one of us (J. E.) in approximately 50 cases and has been found to have all the properties that anaesthetists have long been waiting for. The induction was pleasant for both anaesthetist and patient, and with only a gas-oxygen-isopropyl-chloride sequence the most resistant patient could be smoothly led to the deepest plane of anaesthesia without cough or struggle. This anaesthetic seemed to be equally successful for both major and minor surgery; good muscular relaxation was provided and recovery was both rapid and pleasant. It was noticed that cardiac irregularities occurred, but, as these are not uncommon with sodium thiopentone, "trilene," and cyclopropane, they were disregarded. In order to avoid these irregularities, several patients were induced with gas, oxygen, and ether, and then a change was made to isopropyl chloride, but cardiac irregularities were still noticed in each case, though the patient suffered no ill effects. Unfortunately, a case of complete circulatory failure occurred.

The patient, a man aged 48, was a case of moderately severe thyrotoxicosis. Before operation he had had five weeks' rest in bed and three weeks' premedication with Lugol's iodine. Electrocardiograms taken three weeks before operation showed sinus tachycardia but no evidence of myocardial damage. Under treatment he had gained 5 lb. (2.3 kg.) in weight and his pulse rate fell from a range of 120-110 to 90-80. For the induction of anaesthesia the nitrous-oxide-oxygen-isopropyl-chloride sequence was used. The induction was very smooth and quiet. The patient's colour was good throughout and at no time was there any indication that some difficulty might arise. An endotracheal tube was passed very easily and the patient taken into the theatre. Just 10 minutes after

the induction was started, as the patient was being lifted on to the table, he gave a slight cough and his colour changed to ashen grey; he was found to have complete cardiac arrest. Controlled respiration with oxygen was continued throughout the attempts to restore him. Cardiac massage with intracardiac injections of adrenaline and procaine were given, and after 45 minutes the heart was restarted, but he died a few hours later (Roualle, 1950).

After this experience it was decided that electrocardiographic records should be obtained during the administration of that anaesthetic. For this, two healthy young men were chosen. Only nitrous oxide, oxygen, and isopropyl chloride were used.

Case 1.—The patient was a man aged 31, and the operation was for the removal of a semilunar cartilage. The preliminary record was normal (Fig. 1); thereafter records were taken at approximately five-minute intervals, and more often when the pulse was irregular (Fig. 2). After five minutes Lead II showed a regular rhythm, but with suppression of P waves and depression of the S-T interval; at 11 minutes a curious rhythm had developed with dissociation of the auricular and ventricular elements. The P waves were absent for several beats and then appeared with no constant relation to the QRS complex; there was a high degree of A-V block and possible nodal rhythm. At 17 minutes the rate was 200 a minute, and there were multifocal ventricular extrasystoles; at 19 minutes the rate was 100 and irregular, with absent P waves, suggesting auricular fibrillation. A continuous record was then taken, which showed variations between multiple ventricular extrasystoles to a coarse auricular fibrillation. Five minutes later he reverted to a normal rhythm, which continued to the end of the operation.

Case 2.—This patient was a man aged 25, and the operation was for the repair of the flexor tendons of the right hand. A normal record (Fig. 3) was obtained before the administration of the anaesthetic. Under the anaesthetic he showed less severe changes than the first patient, but (Fig. 4) at five minutes the rate was 120 a minute, with multiple extrasystoles and depression of S-T intervals in some complexes. Extrasystoles were still appearing in the record taken at seven minutes. At 10 minutes the pulse rate had dropped to 60 and was still slightly irregular, but there were normal contractions. At 25 minutes and at the end of the operation, after 45 minutes' anaesthesia, the rhythm was normal.

FIG. 1.—Case 1. Pre-anaesthetic record, normal tracing.

FIG. 2.—Case 1. Consecutive records while under anaesthesia. (a) Depression of S-T interval and absent P waves. (b) Dissociation of P waves and QRS complexes. Possible nodal rhythm. (c) Multifocal ventricular extrasystoles; rate 200. (d) Auricular fibrillation; rate 100. (e) Ventricular systoles, with two beats showing increasing P-R interval. (f) Coarse auricular fibrillation. (g) Reversion to normal rhythm.

FIG. 3.—Case 2. Pre-anaesthetic record, normal tracing.

FIG. 4.—Case 2. Consecutive records while under anaesthesia. (a) Ventricular extrasystoles with depression of S-T intervals in some complexes; rate 120. (b) Ventricular extrasystoles with suggestion of coupling. (c) Normal rhythm. (d) Patient "light." Recurrence of extrasystoles, without depression of S-T intervals. (e) Normal rhythm. (f) Normal rhythm.

There is felt to be evidence that isopropyl chloride exerts a direct toxic action on the myocardium, and extreme caution should be shown in its use. Flagg (1939) reminds us that too many people have tried too often to avoid the use of ether, and it is open to question whether, perchance, in casting out the admittedly unpleasant devils of ether and chloroform we are not making way for seven other far worse devils.

Summary

The pleasant qualities of isopropyl chloride are emphasized.

The high incidence of cardiac irregularities are noted and a death under this anaesthetic is recorded.

Electrocardiographic studies showing severe though temporary changes during the administration of the anaesthetic have been made.

REFERENCES

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Dextran has already received some notice as a possible substitute for plasma in transfusions. It is a complex gummy carbohydrate synthesized by certain bacteria from glucose, and according to a recent press report plans are now going forward for its commercial production. Meanwhile laminarin, a polysaccharide from seaweed, is also under investigation as a plasma substitute and as a replacement for the talc of surgical powder. It is extremely similar to ordinary starch in chemical composition, being largely composed of glucose units linked in chains, but the points of glycosidic linkage differ in the two substances. There are five possible points on the glucose molecular ring at which other glucose molecules can be attached: in ordinary starch, positions 1 and 4 on opposite sides of the ring are so used, whereas in laminarin it is positions 1 and 3 which form the links. Dr. F. M. Woodward, director of the Institute of Seaweed Research, estimates that, if all the 200,000 tons of brown seaweed annually available round Scottish coasts were harvested, there could be a yearly production of 40,000 tons of laminarin. At the same time about 30,000 tons of mannitol would be available, and roughly the same amount of alginic acid, used for making synthetic fibres for the textile industry.

RAISED BLOOD PYRUVIC ACID LEVEL IN DIABETIC ACIDOSIS THE VALUE OF COCARBOXYLASE IN TREATMENT

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Ketosis is a familiar early complication of severe and uncontrolled diabetes mellitus: its causation is understandable, but the steps by which, unchecked, it progresses to coma and shock are not all understood. Usually the standard treatment with insulin and fluids will rapidly resuscitate a patient from diabetic coma: but recovery may be slow or even fail to take place if treatment has been delayed. Prolonged severe diabetic ketosis is evidently complicated by functional disturbances other than those reversible by insulin. One such complication which has recently been clarified is the depletion of potassium and phosphates in the tissues (Guest, 1942; Martin and Wertman, 1947). That disordered carbohydrate oxidation may be another is suggested by the recent finding of a raised pyruvic acid level in the blood in diabetic acidosis (Markees and Meyer, 1948; Markees, 1949).

Pyruvic acid is believed to occupy a central position in the metabolism of carbohydrates; it is an intermediate product in the body's oxidation of these and other metabolites. The first step in the oxidation of pyruvic acid is effected by the pyruvic oxidase enzyme system, which is active only in the presence of certain co-enzymes, including cocarboxylase (Banga, Ochoa, and Peters, 1939). Accumulation of pyruvic acid in the blood suggests a failure of this enzyme system, as is the case, for example, in aneurin deficiency, which results in lack of cocarboxylase (vitamin B₁ diphosphate).

Markees and Meyer (1949) and Boulin *et al.* (1949) have suggested that the administration of cocarboxylase may be a useful supplement to the standard treatment of diabetic coma. They have claimed that the addition of cocarboxylase hastens the recovery from diabetic coma in alloxan-diabetic rabbits (Markees, 1949) and in some human cases (Markees and Meyer, 1949; Boulin *et al.*, 1949), but control data are not given.

This report presents the results of testing the above claims both in alloxan-diabetic rabbits and in four acidotic diabetic patients. Control observations of the rate of recovery under standard treatment have been compared with the results obtained when this treatment is supplemented by cocarboxylase and riboflavin as advocated by Markees and Meyer (1949).

Method

I. Animals

Plan.—After the induction of alloxan diabetes the rabbits were observed for the development of diabetic acidosis. Eight to ten days after the administration of alloxan a number of the rabbits which had become diabetic gradually passed into a phase of progressive