blood differed from that found when treatment was by a single dose of 2 g. However, the effect on the blood and urine sugars was the same in both cases.

Analyses of plasma amino-acid nitrogen and inorganic phosphorus indicate that tolbutamide has a mode of action different from that of insulin.

No toxic effects due to tolbutamide were observed.

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HALOTHANE: ITS USE IN CLOSED CIRCUIT

BY

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This paper describes experience of the use of halothane ("fluothane") in a closed circuit. Others (Johnstone, 1956; Bryce-Smith and O'Brien, 1956) have reported on its open and semi-open administration. Halothane was given from a standard Marrett apparatus to over 1,550 cases during a period of nine months.

Preliminary Trial

Halothane was placed in the large ether jar of a standard Marrett machine. The flow of gas was usually 400–500 ml. of oxygen per minute. The level of liquid in the jar was not kept constant, but this made no noticeable difference to the control setting until the level fell below 2 fl. oz. (57 ml.).

The ether control on the Marrett apparatus is divided into four divisions. During the travel of the control knob (see Diagram) from "off" to " $\frac{1}{2}$ on" (the first two divisions on the scale) only the patient's breath passes into the jar. The gases from the flowmeters are delivered direct to the inlet unidirectional valve. This range of the control is equivalent to the full range of closed-circuit vaporizers on most other machines.

To ascertain the relative strength of halothane, a personal trial was undertaken. With half a litre of oxygen a minute

and the control set at three-fourths of the first division (see Diagram), no irritant effect was noticed; nor the buzzing in the head so characteristic of nitrous oxide and other inhalation anaesthetics. Loss of consciousness, accompanied by marked jaw relaxation and loss of corneal reflex, took three minutes, and recovery was complete in five minutes, with no subsequent headache or nausea. With the control set at the second division (full on for the closed circuit) the vapour produced coughing, but was soon tolerated, and loss of consciousness took one minute, with 10 minutes for recovery and again no headache or nausea. It was therefore clear that the concentration was safe and that halothane was likely to be most useful for inductions, particularly if an intravenous anaesthetic was contraindicated as in the very old or emergencies; it would probably also be useful for resistant dental cases, provided only a few breaths were given to allow the third stage to be established. It remained, however, to find out if there was any accumulation in the body after a long administration in closed circuit, or if there was any "build up" of concentration in the breathing circuit.

Induction and Maintenance

Although premedication causes respiratory depression, for the patient's comfort the premedication usual at this hospital was continued—that is, "omnopon," $\frac{1}{2}$ gr. (22 mg.), and scopolamine, 1/150 gr. (0.43 mg.), for the healthy adult up to 56; morphine, $\frac{1}{2}$ gr. (10 mg.), and atropine, 1/100 gr. (0.65 mg.) were used for the elderly, and atropine, 1/100 gr. (0.65 mg.), for the bad risk and those over 70.

As halothane itself is known to depress respiration, for induction a dose of thiopentone varying from 0.15 to 0.25 g. was used in healthy adults instead of the usual 0.5 g. The mask was then placed on the face with the halothane control at three-fourths of the first division and an oxygen flow of half a litre a minute. Sometimes the respiratory depression from the thiopentone persisted when the halothane was added, though normal respirations would return immediately after a painful stimulus or pulling on the chin. At this stage a tough individual might become restless, but if the control was put to the second division (full on) he would quieten after three or four breaths, although he might cough. With a strong vapour patients might cough, but laryngeal spasm was never encountered, nor was it possible to produce one purposely—a most useful attribute.

For a major abdominal operation the control was then slowly advanced until the abdomen relaxed. At this stage depth of respiration was normal for the closed circuit, and blind or direct intubation could be performed early owing to the complete relaxation of the jaw and larynx. After this all cases were conducted on the principle of physiological breathing, full relaxation for all abdominal operations always being obtainable. At the start of the series D-tubocurarine was used in doses of 5–10 mg. for abdominal operations, but with further experience this proved unnecessary; also, apnoea often occurred and the systolic pressure might fall as low as 45 mm. Hg, although this would rise quickly after an injection of atropine, 1/100 gr. (0.65 mg.).

The maintenance of anaesthesia was usually with the control set at three-fourths of the first division 2% halothane, and at the first division 2.4% for abdominals. A setting beyond the first division was always too much. The margin between light and deep anaesthesia was narrow, so if the patient became too "light" a few breaths of a slightly stronger concentration would soon settle him; but unless this concentration was very soon reduced apnoea developed. If from overdose respiration became too shallow recovery occurred quickly on cutting down or turning off the halothane. On closure of the peritoneum the halothane and soda lime were switched off, and nitrous oxide, oxygen, and air substituted for the remainder of the operation.

The patients all recovered quietly, with a remarkable lack of post-operative vomiting and nausea, and were quite obviously little affected by their operation when seen the following day. There was never the slightest suggestion of

accumulation of the drug : all patients recovered their jaw tone and swallowing reflexes within a few minutes of leaving the theatre, however long their anaesthesia. Nor was there any "build up" of concentration during administration, as the drug had to be given for the most part continually, otherwise the patient quickly showed signs of becoming "light." Consumption varied between 4 ml. and 6 ml. per hour. Considering the high price of halothane, this is very economical compared with open and semi-open administrations.

Discussion

The fact that halothane produces a fall in blood pressure gives rise to no anxiety unless there is serious loss of blood

Sketch of the apparatus.

or D-tubocurarine has been given. For this reason halothane should not be used in operations where blood loss is inevitable, such as caesarean sections and some orthopaedic operations, unless a transfusion is started at the outset. Further, if an unexpected loss of blood occurs during an operation under halothane anaesthesia, the blood must be replaced before the patient is returned to the ward. In operations where a raw surface is left—for example, tonsillectomy, cholecystectomy, etc.—such areas were often found to start oozing again when the halothane was turned off. I suggest therefore that in these cases the halothane should be turned off for several minutes so that any oozing can be dealt with, and then turned on again if necessary to produce relaxation for closure of the peritoneum; otherwise there is a risk of reactionary haemorrhage. This vasodilatation bears no relation to the level of the blood pressure and also occurs during induction, when again the halothane concentration in the blood is low. On the other hand, during surgical anaesthesia, when the halothane concentration is higher vasoconstriction occurs, giving a relatively bloodless field. Again this is unrelated to the blood pressure.

In the series described 1 in 400,000 adrenaline in normal saline was used for infiltration in mastectomies, thyroidectomies, and abdomino-perineal operations, etc., in quantities ranging from 200 to 400 ml. without effect on the pulse. No adverse action on the heart due to halothane was noted, although some of the cases were known to have conditions such as recent rheumatic fever, mitral stenosis, and auricular fibrillation.

Halothane is most useful for the induction of bad-risk emergency cases, because it is non-irritant and the passage through the second stage until the jaw and larynx are sufficiently relaxed for intubation is rapid and tranquil.

With increasing experience the use of D-tubocurarine with halothane was abandoned, as adequate abdominal relaxation could be obtained when using the closed circuit and easily maintained on a low concentration 2–2.4% of anaesthetic without recourse to controlled respiration. This property of

halothane has proved most useful in the conduct of such difficult minor operations, from the anaesthetist's point of view, as gynaecological examinations. The legs of such patients can be relaxed for the lithotomy position within a minute or two and the abdominal wall relaxed for ease of examination. Versions are also easy to perform. Likewise cystoscopies in males are quickly performed without a mobile patient or unnecessarily deep anaesthesia. Being non-explosive and non-inflammable, halothane simplifies the anaesthetic technique if diathermy is needed.

Halothane has been most useful for bronchoscopies and oesophagoscopies. For the former a "sleep" dose of thiopentone (0.1–0.2 g.) is given, followed by halothane and oxygen for about three minutes. A bronchial sucker tube is then inserted 3 in. (7.6 cm.) into the trachea and anaesthesia is maintained by insufflation with halothane and oxygen. This results in quiet respiration and no coughing, and obviates the need for local analgesics. My experience of halothane for chairside anaesthesia in dentistry is limited, but it has proved most useful in hastening the resistant patient into the third stage when using nitrous oxide and oxygen. Only a few breaths should be given, so that the reflexes return quickly.

Lastly, halothane's chemical reactions must be briefly mentioned. It is perfectly stable and does not react with soda lime. Although halothane has been used continuously for the past nine months in a Marrett apparatus, there has been no chemical damage to the mechanism of the machine, nor has there been any noticeable effect on the corrugated tubes or reservoir bag. Halothane is known to attack metals, particularly aluminium and tin, in the presence of moisture, but my experience suggests that if the apparatus is made of chrome, nickelled brass, and copper these reactions are of no consequence.

Summary

The administration of halothane ("fluothane") in closed circuit with a Marrett apparatus for both induction and maintenance of anaesthesia is reported, and the techniques are described. Halothane was used to anaesthetize over 1,550 unselected cases during a period of nine months. There were no deaths during anaesthesia or in the post-operative period.

Anaesthesia was characterized by a smooth induction, excellent relaxation, without the need for relaxants, and the rarity of post-operative nausea and vomiting and shock. Halothane also proved particularly useful for minor procedures where maximum relaxation is required, such as gynaecological examinations and versions, and for various endoscopic examinations. Being non-inflammable, halothane is safe to use with diathermy. No corrosive action on the Marrett apparatus used in the trial was observed.

So far as disadvantages are concerned, profound respiratory depression was invariably due to overdosage; this can quite easily be avoided, as only a moderate dose is required to obtain excellent abdominal relaxation. The fall in blood pressure caused by halothane constitutes no hazard unless aggravated by blood loss or the use of D-tubocurarine. The latter was found to be unnecessary, as relaxation was excellent without it. When halothane is turned off previously dry raw surfaces tend to ooze. This must be guarded against because of the possibility of unseen reactionary haemorrhage, and a method of doing so is suggested.

The indications and contraindications for the use of halothane are discussed, and it is concluded that the drug can be successfully and safely used in a standard closed-circuit apparatus.

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SARCOSPORIDIOSIS IN MAN WITH PERIARTERITIS NODOSA*

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Sarcosporidiosis is a very common protozoal parasitic infestation of muscle fibres in animals in this and many other countries; it has rarely been observed in man. Since its discovery first in mice by Meischer, in 1843, it has been extensively studied in animals.

The life-cycle remains unknown, but the spores are probably ingested in food and eventually gain entry to the striated musculature. There they form large cysts within individual muscle fibres and may attain 5 mm. in length. Each cyst when fully developed shows characteristic division by septa into chambers containing myriads of sickle-shaped spores, which appear to degenerate towards the centre. Infestation has often appeared to be harmless in animals, but when heavy it has produced serious pathological effects and death. Transmission to other animals is probably due to rupture of cysts into the alimentary canal and faecal contamination of food thereby (Scott, 1943). We suggest that the disease is conveyed from animals to man by means of contamination of uncooked food by animal faeces.

We have reviewed the human cases reported, and we accept the eight cited by Feng (1932), who added a case of his own, two reported by Vuillemin (1902), and one each by Lorenz (1904), Hewitt (1933), Gilmore *et al.* (1942), Kean and Grocott (1945), Pugh (1950), and Mackinnon and Abbott (1955).

An eighteenth case is here reported because of the apparent rarity of the condition in man and also because the parasitic infestation was associated with various pathological lesions, including periarteritis nodosa, which have not been described before. In addition, no previous case has come to full necropsy examination. A complement-fixation test devised by Awad and Lainson (1954) has been used in the present case for the first time in establishing the diagnosis during life.

Case Report

A European official aged 60, retired from India before 1939, was well until April, 1953. Suddenly he collapsed,

*Based on papers read before the Wessex Physicians Club and the Association of Clinical Pathologists.

almost losing consciousness, with, however, no specific weakness, and next morning he had recovered fully. Eight months later he suddenly lost the use of his right arm, and examination revealed diminished power there with increased tendon reflexes but no sensory changes. Complete recovery gradually took place during the next two weeks. One month later a similar sudden weakness of the left arm occurred and again recovery was rapid. Complete physical examination then proved normal, and the B.P. was 140/80. During the next five months exertional dyspnoea began and rapidly increased. Chest radiographs revealed scattered ill-defined but discrete opacities in both lung fields, suggestive of disseminated vascular lesions; biopsy of a pectoral muscle was therefore performed. Subsequently a right homonymous hemianopia developed with right hemiparesis, headache, and mental deterioration. The signs of congestive cardiac failure progressed, and he died on June 21, 1954.

Laboratory Investigations.—No abnormality was found in the blood count and differential count on any occasion. The urine was repeatedly normal. The C.S.F. was normal. E.S.R. was 30 mm. in one hour, rising later to 80 mm. in one hour; serum albumin, 3.4 g. per 100 ml.; serum globulin, 3.0 g. per 100 ml.; liver-function tests normal; W.R. negative; serum complement-fixation test for sarcosporidiosis, positive 1:32; complement-fixation test for toxoplasmosis negative.

Three series of electrocardiograms taken in the last week of his life showed combined heart strain.

Muscle Biopsy.—No evidence of periarteritis nodosa was found, but a number of cystic structures were seen within individual muscle fibres (see Fig.). Each cyst had a delicate

Left-side pectoral muscle with sarcocyst. Note very thin capsule and internal septa. A thin rim of sarcoplasm still surrounds the parasite. (H. and E. $\times 145$.)

hyaline wall and contained a large number of minute basophilic sickle-shaped spores. In longitudinal section the cysts were seen to be at least 1 mm. in length and to be divided by septa into separate chambers. The spores seemed to be produced at the periphery and to degenerate towards the centre of the cyst. No inflammatory reaction was found. These appearances are typical of sarcosporidium (*Sarcocystis*).

Necropsy Findings

Necropsy confirmed that death was due to congestive right heart failure. The heart was moderately enlarged owing to left and right ventricular dilatation. Attached to the base of the tricuspid valve and spreading on to the ventricular and auricular walls was an enormous mass of friable grape-like vegetations; smaller vegetations arose in the pulmonary conus and from the papillary muscles. No vegetation was found within the left heart, but the interventricular septum showed fibrous scarring. The lungs were bulky, and all lobes contained small, firm, often yellowish stellate scars, associated with which were multiple thrombi in the branches