

## EVALUATION OF FLUOTHANE FOR CLINICAL ANAESTHESIA

C. R. STEPHEN, M D, D C GROSSKREUTZ, M D, J H A LAWRENCE, M D,  
L. W. FABIAN, M.D, M. BOURGEOIS-GAVARDIN, M D, and J. COUGHLIN, M D \*

PHARMACOLOGICAL DEVELOPMENTS are unfolding so rapidly in the realm of anaesthesia that almost every week a new drug is made available for study and trial. With the increasing use of the cautery and the concerted effort to avoid explosions, a marked need has arisen for a safe, potent, non-inflammable inhalation anaesthetic drug. Robbins (1) in 1946 investigated a number of non-explosive fluorinated hydrocarbons in the laboratory and concluded that six might be of clinical value. No further work was done until 1953, when Krantz *et al.* (2) reported on the safety of a fluorinated ethyl vinyl ether. Unfortunately, this compound was explosive in anaesthetic concentrations (3). Meanwhile, Suckling in England, while screening non-explosive fluoride compounds, synthesized 2-bromo-2-chloro-1,1,1-trifluoroethane ( $\text{CF}_3\text{CHClBr}$ ). This compound, called Fluothane, was investigated pharmacologically by Raventos (4), who found it to be a potent and safe anaesthetic drug in several species of animals. Within the last year several clinical reports attesting to the value of this drug have been published (5, 6, 7, 8).

Fluothane is a clear, colourless liquid with a sweet, pleasant odour resembling trichlorethylene or chloroform (Table I). The boiling point ( $50.2^\circ\text{C}$ .) renders

TABLE I  
PHYSICAL PROPERTIES OF FLUOTHANE

Appearance	Colourless, clear
Odour	Sweet, pleasant
Molecular weight	197.39
Boiling point	$50.2^\circ\text{C}$
Specific gravity	1.862 at $22^\circ\text{C}$
Oil/water solubility	330
Vapour pressure	243 mm at $20^\circ\text{C}$

vaporization by the open drop technique feasible and practical. The compound is non-inflammable and non-explosive in any concentration with air or oxygen. Although decomposed slowly by light to hydrochloric acid and phosgene, the drug is stable at room temperatures when treated with thymol, 0.01 per cent, and kept in light-resistant containers. It does not form toxic products with soda-lime in the presence of heat and can be used safely with the carbon dioxide absorption technique.

### LABORATORY FINDINGS

Fluothane came to our attention in February, 1956.† Preliminary laboratory investigations in dogs and monkeys (9) confirmed many of the findings of

\*From the Division of Anaesthesia, Duke University School of Medicine, Durham, North Carolina.

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Raventos (4). The drug was extremely potent. It could produce severe respiratory depression and marked hypotension in three to five minutes when administered rapidly. However, respiratory paralysis due to over-dosage always preceded cardiac arrest. Fluothane did sensitize the myocardial conduction mechanism to epinephrine-like compounds, but peripherally acting vasopressors like methoxamine and neosynephrine could be injected safely with normal responses. The administration of d-tubo curarine chloride to a dog anaesthetized with Fluothane resulted in profound cardiovascular collapse, and yet succinylcholine could be injected with the anticipated normal effect. Chronic administration of Fluothane to seven dogs and two monkeys for 24 hours over a period of six days showed no advanced histological changes in any organs. In several of these animals there was some pallor of the hematoxylin-eosin stain in the areas surrounding the central vein of the liver lobules. This finding indicated that close attention would have to be directed to the effect of this drug on liver function. Such work is in progress at the moment.

#### CLINICAL INVESTIGATION

Fortified with the above laboratory data, staff and resident physicians administered Fluothane to 500 patients, varying in age from 8 months to 73 years (Table II). Although 63 per cent of patients were judged to be in good physical

TABLE II  
AGE DISTRIBUTION OF PATIENTS RECEIVING FLUOTHANE

Age (years)	Number of patients	Per cent
Less than 10	43	8.6
11-20	35	7.0
21-30	104	20.8
31-40	139	27.8
41-50	97	19.4
51-60	45	9.0
Over 60	37	7.4

condition, the drug has been employed successfully in patients with asthma, pulmonary emphysema, diabetes, moderate hypertension, arteriosclerotic heart disease and advanced carcinoma. Forty-three patients were considered to be poor risks. All types of surgical procedures (Table III) lasting from 10 minutes to 8½ hours (Table IV) have been included in the series

TABLE III  
VARIETY OF OPERATIONS PERFORMED WITH FLUOTHANE

Operative site	Number of patients	Per cent
Head and neck	114	22.8
Trunk and extremities	193	38.6
Intrathoracic	53	10.6
Intra-abdominal	99	19.4
Perineum	39	7.8
Cancelled	2	0.4
Major operations	265	53.0
Minor operations	235	47.0

TABLE IV  
DURATION OF ANAESTHESIA TIME WITH FLUOTHANE

Duration of anaesthesia	Number of patients	Per cent
Less than 1 hour	107	21.4
Less than 2 hours	157	31.4
Less than 3 hours	74	14.8
More than 3 hours	162	32.4

The premedication normally ordered was not changed drastically for patients receiving Fluothane. A short-acting barbiturate two hours preoperatively, followed by a narcotic (meperidine or morphine) one hour before operation, along with an anticholinergic drug shortly before induction, was the rule. It was noted that marked respiratory depression during anaesthesia was more prone to occur in patients who manifested a profound reaction to narcotics. The situation was similar to that which is seen with cyclopropane anaesthesia.

Atropine, 0.6 mg., and Antrenyl®, 0.6 mg., were believed to be important premedicant drugs, as they tended to minimize the incidence of bradycardia during operation.

#### *Induction*

Induction by the open drop technique was performed in 27 children. The vapours were accepted readily, but a short excitement period lasting about one minute usually occurred. Coughing, vomiting and laryngospasm were noticeably absent. The third stage was achieved rapidly in two to five minutes with Fluothane dropping at a rate of 30 to 40 drops per minute. With added oxygen flowing under the mask, eight children were maintained for two to three hours on 10 to 12 drops per minute for orthopaedic and plastic procedures. Other children were maintained with an endotracheal non-rebreathing valve technique or with the non-rebreathing mask. Hypotension and bradycardia have not been noted in children. Deep planes of anaesthesia were signified by progressive intercostal paresis.

In 86 (17 per cent) of the patients induction was achieved in a semi-closed circle absorption system, employing a four litre per minute flow of oxygen or two litres each of nitrous oxide and oxygen to vaporize Fluothane in a concentration of 3.5 to 4.0 volumes per cent. A short but intense excitement period was seen in the majority of these patients, but could be circumvented by administering a sleeping dose of an ultra-short-acting barbiturate (surital sodium, 75-200 mg.) prior to application of the mask. The majority of patients in this series (382) received this latter method of induction. In order of preference, Fluothane was vaporized from a Boyle "Trilene" bottle, a Foregger "vinethene" bottle, a Foregger "copper kettle" and a standard Heidbrink ether bottle with wick in place. All but the latter vaporizer were calibrated for flows of 4 litres per minute.

The rapidity of induction, associated with the early obtundation of pharyngeal and laryngeal reflexes, the masseter muscle relaxation and the absence of salivary secretions were remarkable in all patients. An oral pharyngeal airway

could be inserted in two to three minutes and endotracheal intubation accomplished, if performed with dexterity, in four to six minutes, without cessation of spontaneous respirations. The limitation to atraumatic, smooth intubation lay primarily in the rapidity with which anaesthesia lightened during the technical insertion of the tube. In 45 to 60 seconds the patient could be phonating and gagging. However, vomiting occurred during induction in only two patients. This reaction seldom provoked a laryngospasm and, on application of the mask, deeper planes of anaesthesia were obtained rapidly. Endotracheal intubation was employed in 276 (55 per cent) of patients. Of this group, 54 per cent were intubated with Fluothane alone. In the remainder, because of the above limitations, succinylcholine, 20 to 60 mg, was employed to facilitate insertion of the tube. Resumption of spontaneous respiration after the succinylcholine apnoea occurred smoothly and within the anticipated time period.

The signs of deepening anaesthesia were related primarily to the respiratory and cardiovascular systems. The classical signs of intercostal paresis and paralysis were similar to those seen with ethyl ether, except that with Fluothane they occurred much more rapidly. Respiratory paralysis due to Fluothane was seen rarely and easily reversed by lightening the plane of anaesthesia.

Developing hypotension was also considered to be a sign of increasing depth of anaesthesia and usually could be reversed by reducing the concentration of Fluothane. Since blood pressure is an important clinical reflection of cardiovascular function, careful attention was devoted to the incidence of hypotension with Fluothane. During induction significant fall in blood pressure occurred in 41 per cent of the patients (Table V). Figure 1(a) shows the anaesthetic record

TABLE V  
DEGREE OF SIGNIFICANT HYPOTENSION DURING INDUCTION WITH  
FLUOTHANE

B P fall (mm. Hg)	Number of patients	Per cent
20-30	87	19 0
30-40	55	11 3
40-50	27	5 5
50-60	16	3 2
More than 60	10	2 0
Total	195	41 0

of a 55-year-old patient undergoing a thoracotomy and illustrates the typical hypotensive phenomenon. The prior administration of an ultra-short-acting barbiturate did not influence the incidence of hypotension. In all but sixteen patients the blood pressure returned to satisfactory levels with a lightening of the plane of anaesthesia, or associated with operative manipulation. Ancillary measures were judged necessary for the sixteen patients: Antrenyl® was administered to eight; vasopressor drugs to five; and for three Fluothane was discontinued temporarily. The exact cause of this hypotension is unknown, but it is interesting that patients receiving Fluothane had warm, dry extremities with full pulses and dilated veins, similar to what is seen following administration of chlorpromazine. This peripheral vaso-dilatation appeared to be a constant phenomenon.

Bradycardia was not common during induction. Only fourteen patients showed

a decrease in pulse rate of more than twenty per minute. The insistence on adequate doses of anticholinergic drugs given shortly before induction may account for this finding, which is somewhat dissimilar to that noted by others (8). Tachycardia was a rare occurrence.

*Maintenance*

In practically all adults, anaesthesia was maintained with equal flows of nitrous oxide and oxygen, at a rate of 4 litres per minute, as outlined above. This semi-closed technique was chosen arbitrarily and in an effort to maintain constancy of some factors during the evaluation. Satisfactory anaesthesia for most operations could be attained with a concentration of 0.8 to 1.5 volumes per cent of Fluothane being delivered from the vaporizer. The only supplementary drug employed in this series was succinylcholine. It was considered a useful adjunct to provide needed relaxation for upper abdominal surgery and to obtund or prevent bucking associated with hilar manipulation during intrathoracic operations. Fluothane itself provided sufficient relaxation for other surgical operations.

As a rule surgical stimulation could be tolerated within three to eight minutes

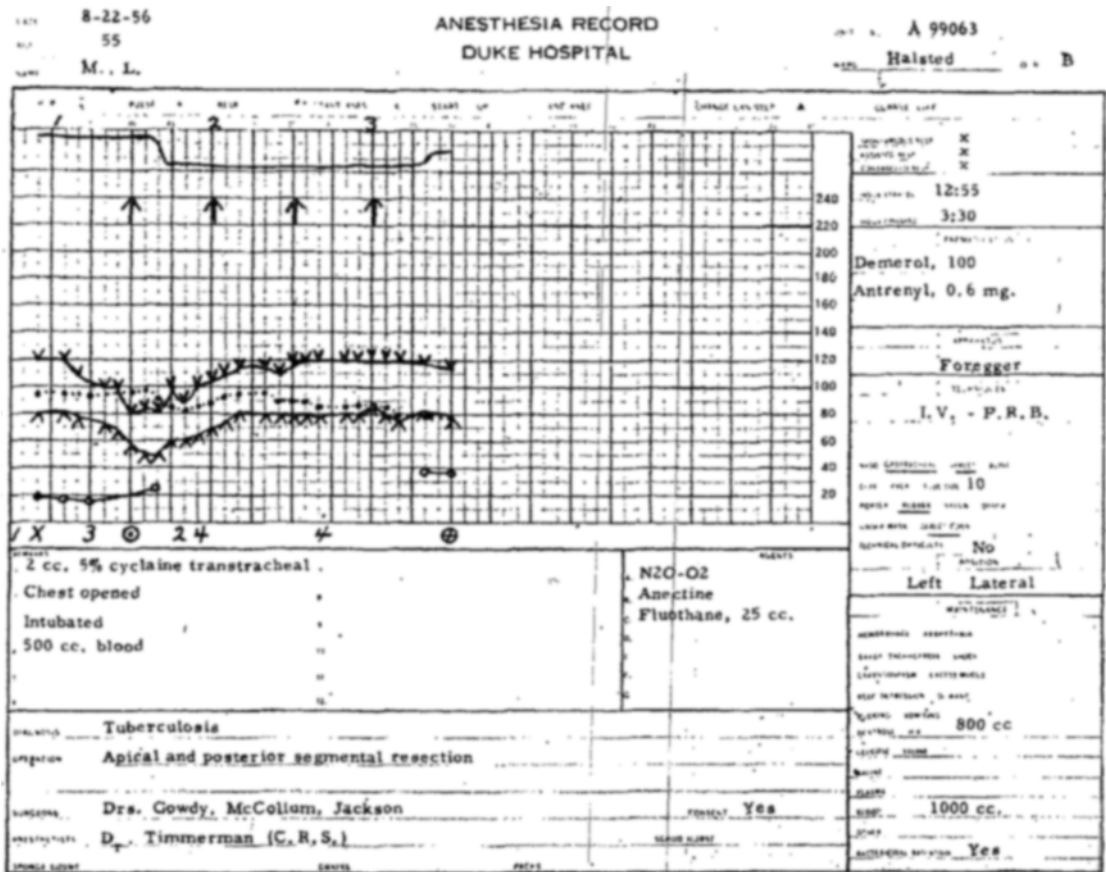


FIGURE 1(a) Anaesthetic record of 55-year-old male undergoing apical and posterior segmental resection of lung for tuberculosis. Anaesthetic drugs: surital sodium, 140 mg., cyclaine, 2.0 cc. 5% solution transtracheal, nitrous oxide, 2 litres, oxygen, 2 litres, Fluothane, succinylcholine, 200 mg.

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## Thoracotomy for Pulmonary Tuberculosis

Surital, 140 mg., N<sub>2</sub>O-O<sub>2</sub>, Fluothane, Anectine, 200 mg.

<u>Time</u>	<u>pH</u>	<u>pCO<sub>2</sub></u>	<u>O<sub>2</sub> Sat. %</u>	
12:30	7.47	32.8	96	Control awake
1:35	7.40	38.8	100	Spon. resp. B. P. 82/50
2:30	7.61	19.6	100	Cont. resp. 45 mins.
3:10	7.51	28.2	100	Cont. resp. Closing
3:40	7.44	39.6	100	Tube out Coughing

FIGURE 1(b) pH, pCO<sub>2</sub> and oxygen saturation before, during and at conclusion of thoracotomy. Respirations controlled while in chest

of beginning anaesthesia. The plane of anaesthesia could be altered with three or four respirations and fineness of control was limited only by the inadequacies of the vaporizers employed. The potency of the drug could be both a bane and a blessing. Rapidity and ease of control was offset by ease of over-dosage.

"Surgical" anaesthesia in this series was associated with depression of respiratory rate and depth, but particularly the latter. "Assisted" respirations were employed in nearly all cases. It was interesting to note in many patients how easily complete control of respirations could be assumed when assistance was begun. In this way the drug resembled cyclopropane. The anaesthesiologist had to watch the patient closely when controlled respirations were first instituted, because an increased depth of anaesthesia often developed in rapid fashion. Figure 1(b) shows that a tendency to alkalosis occurred when controlled respirations were employed. As with any other anaesthetic drug, if adequate alveolar ventilation was maintained, one did not need to fear respiratory acidosis with Fluothane.

In the majority of patients, as illustrated in Figure 1(a), hypotension at the

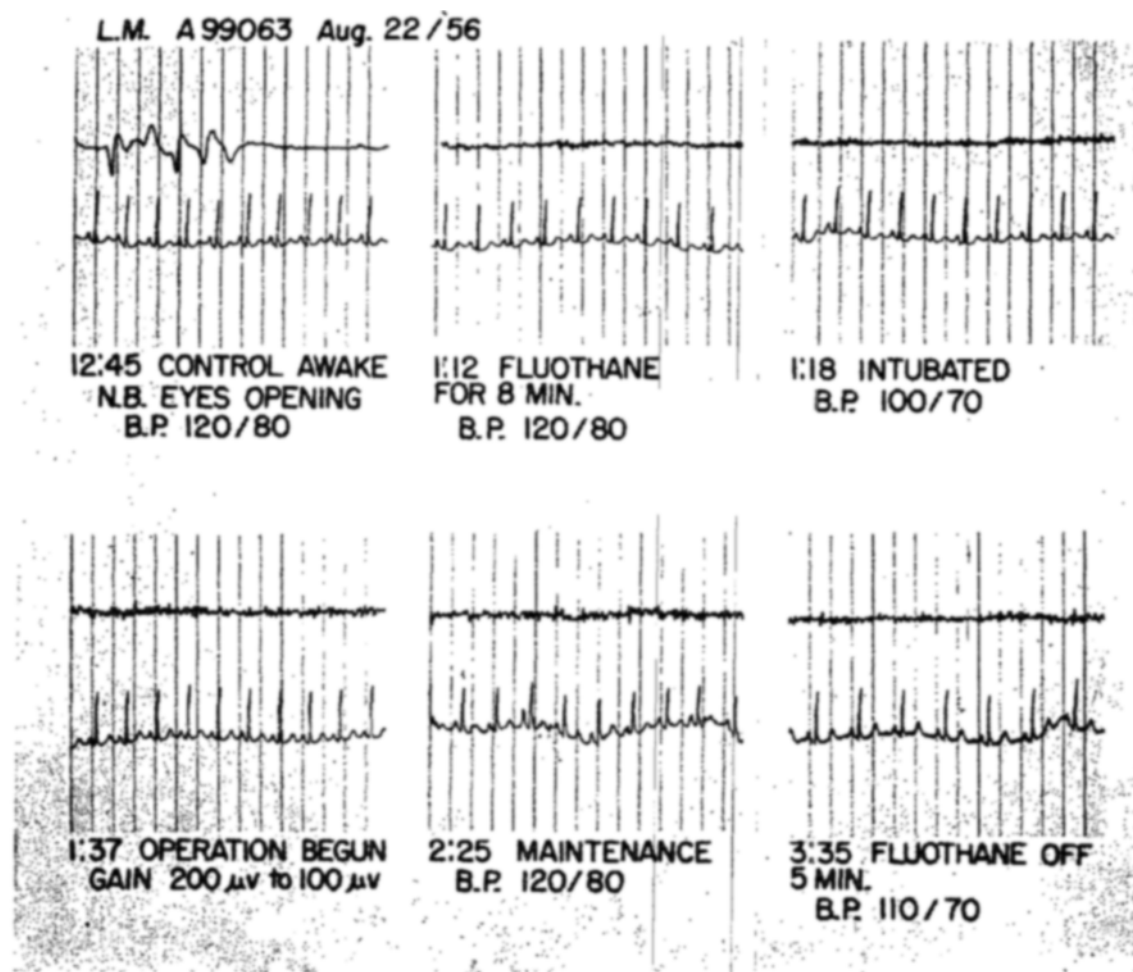


FIGURE 1(c) Electroencephalographic and electrocardiographic tracings recorded during operation on Edin anesthesiograph.

time of induction was corrected, usually spontaneously, during the maintenance period. However, in fifty-six patients (11.5 per cent) of this series a blood pressure fall of 20 mm. Hg or more occurred during operation. In ten patients unreplaced blood loss was judged to be the cause of the drop. Patients anaesthetized with Fluothane appear to be unusually sensitive to bleeding; in this way they resemble patients rendered hypotensive by ganglionic-blocking drugs. This observation reflects the peripheral vaso-dilatation seen clinically. In several patients the hypotension was associated with traction on the upper abdominal contents. This reflex appears to be initiated more frequently with Fluothane than with other drugs. The hypotension encountered required specific pharmacologic therapy in eleven patients. In the remainder the situation was corrected with transfusion or watchful waiting.

Bradycardia was not a problem during maintenance of anaesthesia. In only three patients did the pulse rate fall below 60 per minute.

With a halogenated compound like Fluothane, the possibility of cardiac arrhythmias is very real. In view of that fact that the injection of epinephrine

in the dog anaesthetized with Fluothane could produce ventricular fibrillation, we have avoided this combination. However, epinephrine for subcutaneous haemostasis was injected on four occasions inadvertently in this series, with no resultant clinical arrhythmias.

Continuous electrocardiograms were recorded in thirty patients early in the series. In eighteen patients no changes were seen. Seven developed nodal rhythm, three showed premature auricular contractions and two premature ventricular contractions. Clinical observation in the remainder of the series detected six arrhythmias of ventricular origin. All arrhythmias reverted spontaneously with lightening of the plane of anaesthesia or with improved ventilation. In no patient was it necessary to discontinue the drug administration. Arrhythmias have been noted less frequently as dexterity in administering the drug has improved. Preoperative arrhythmias have not become more serious under Fluothane anaesthesia.

The electroencephalogram was monitored in a number of patients (Figs. 1, 2). With increasing depth of anaesthesia fast activity disappeared and slow, high voltage waves became prominent. A pattern corresponding to Level 3 appeared to provide satisfactory anaesthesia.

Halogenated compounds are particularly prone to disturb liver metabolism or to produce irreversible cellular changes in this vital organ. Unfortunately, none of the laboratory tests available reflects in a convincing or complete manner the true status of liver function. Considerable cellular dysfunction or damage may be present without any objective evidence.

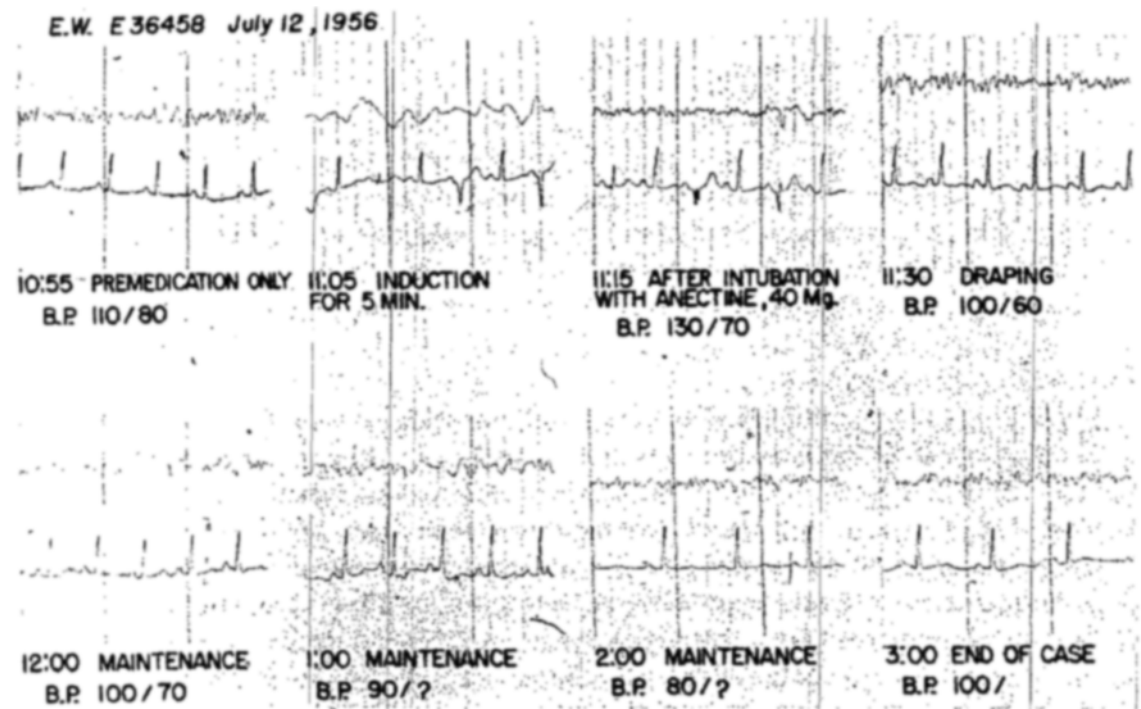


FIGURE 2. Electroencephalographic and electrocardiographic tracing of patient receiving fluothane anaesthesia. N.B. ventricular arrhythmias during induction period, rapid alteration in electroencephalographic patterns.



Recognizing the limitations involved, an attempt was made to assess the influence of Fluothane on liver metabolism. In twenty patients subjected to anaesthesia for two hours or more, blood sugar determinations were made pre-operatively, after one hour of anaesthesia, two to three hours after anaesthesia, and twenty-four hours postoperatively. The respective average blood sugar levels in mg per cent were 106, 104, 111, and 95. In this group Fluothane produced less disturbance in blood sugar levels than most conventional anaesthetic drugs. These results may be a reflection on liver metabolism itself or an indication that stimulation of the adrenal medulla does not accompany administration of this drug.

Of the several liver function tests, the rate of clearance of bromsulphalein dye from the blood stream is as representative as any. In 51 patients who received Fluothane for more than one hour, BSP dye tests were performed 24 hours and 5 days following anaesthesia. Controls consisted of a similar group of patients subjected for more than one hour to ethyl ether, cyclopropane or pentothal, nitrous oxide, meperidine anaesthesia. The results are tabulated in Table VI. Abnormal dye retention was found in both groups. Careful analysis

TABLE VI  
LIVER FUNCTION (BROMSULPHALEIN DYE RETENTION)

More than 5% retention in 45 minutes	Number of patients	Per cent
CONTROLS (51 patients)		
24 hours postoperative	22	43.1
5 days postoperative	7	13.7
FLUOTHANE (51 patients)		
24 hours postoperative	20	39.2
5 days postoperative	6	11.8

of the case reports revealed no specific reasons for the apparent liver dysfunction in these patients, although retention occurred only following extensive surgical procedures. This single test indicated that Fluothane was not more likely to produce hepatic dysfunction than the conventional anaesthetic drugs.

### Recovery

Recovery from anaesthesia was rapid and remarkably free of excitement, even after prolonged administration. Protective reflexes and movement on demand usually returned within five minutes. Full orientation as to time, place and person was present within ten to twenty minutes. Nausea and vomiting occurred in only 6 per cent of patients and was short-lived. Possibly the absence of secretions during operation contributed to the minimal post-anaesthetic vomiting. Shivering was noted in 5 per cent of patients, but was controlled easily. Recovery room nurses were able to return Fluothane patients to the ward much sooner than others.

Postoperative morbidity was minimal in this series. No pulmonary or cardiovascular complications occurred in which Fluothane could be implicated directly.

Five patients died in the postoperative period. One patient undergoing a lobectomy for tuberculosis developed a bleeding diathesis on the operating table which continued postoperatively despite vigorous therapeutic measures. She responded completely following anaesthesia, but developed pulmonary oedema and died 8 hours after operation. One patient died from severe pulmonary interstitial fibrosis 48 hours following a biopsy of the lung under anaesthesia. The other patients died from a cardiovascular accident four days after operation, pneumonia on the eighth day and from a brain tumour on the tenth day.

No deaths occurred during anaesthesia, but cardiac arrest developed in one patient. A 30-year-old white male, considered a good risk, came to the operating room for a right ureteral exploration following persistent right lower quadrant pain. Following a sleeping dose of pentothal sodium, 120 mg., he was induced and maintained with nitrous oxide, oxygen and Fluothane as described above. Endotracheal intubation was facilitated with succinylcholine, 50 mg., and respirations were controlled throughout the operation. After one and a half hours of uneventful anaesthesia, and as peritoneal closure was beginning, there was a sudden absence of pulse and blood pressure. No aortic pulsations were discernible, so an immediate left thoracotomy was performed and the heart found to be in asystole. Spontaneous cardiac rhythm returned one or two minutes after massage had started and the blood pressure rose rapidly to the previous level of 120/80. The patient made an uneventful recovery and suffered no apparent sequelae. It is impossible for us to assess the role of Fluothane in this cardiac arrest. It might very well be incriminated but, unfortunately, similar experiences have occurred in the past in which other anaesthetic drugs have been utilized.

#### DISCUSSION

Whenever a new anaesthetic drug becomes available for clinical trial, the first reports are optimistic, later reports are more guarded in outlook, and finally, after several years, a more accurate assessment evolves. According to time relationships and also the brief experience of the authors, this report is optimistic in nature.

The anaesthesiologist needs a potent, non-inflammable and non-explosive inhalation drug. Fluothane possesses these virtues. In addition, induction of anaesthesia is rapid, salivary secretions are absent, pharyngeal and laryngeal reflexes are obtunded early, moderate degrees of muscular relaxation are provided in "surgical" planes, depth of narcosis can be varied rapidly and easily, and recovery occurs quickly with minimal nausea and vomiting.

The principal remaining mandatory attribute pertains to the *safety* of this compound in clinical practice. Does the administration of Fluothane endanger the life of the patient to a greater degree than drugs presently utilized to produce narcosis? The answer to this question may not be available for several years. However, opinions may be expressed, and ours is that this drug can be employed safely, *if administered properly and accurately*.

Proper clinical administration is related directly to the potency of Fluothane. Concentrations of Fluothane required for induction are 2 to 4 volumes per

cent and those needed for maintenance are 0.5 to 1.5 volumes per cent. The vaporizers at present available on anaesthetic gas machines in the United States, with the possible exception of the Foregger "copper kettle," do not allow one to deliver to the patient these low concentrations in a sufficiently precise manner for safe administration. Modification of present vaporizers, or new vaporizers, which permit variations of concentrations in tenths of volumes per cent are necessary for safe administration of Fluothane.

The potential hazards associated with Fluothane anaesthesia pertain to the respiratory, metabolic and cardiovascular systems. In "surgical" planes of anaesthesia the respiratory centre is depressed so that minute volume is decreased. This property of Fluothane should not be of concern to anaesthesiologists. Most of the drugs employed in daily practice depress respirations either centrally or peripherally. The manual assistance of respiratory exchange to maintain adequate alveolar ventilation should be second nature and as automatic as monitoring the pulse rate and blood pressure.

Interference with liver metabolism and a direct toxic effect on hepatic cells is a potential hazard of Fluothane which has not yet been ruled out. However, laboratory and clinical experiences to date have failed to demonstrate deleterious effects which would prohibit the use of the drug.

The action of Fluothane on the cardiovascular system is an important factor when related to safe usage. Hypotension from any cause is undesirable during operation, except under particular circumstances when it is induced intentionally. The falls in blood pressure seen with Fluothane can increase the hazard to the patient. However, it is our belief that accurate methods of vaporizing this drug will avoid much of the hypotension which is seen. In the present series the incidence of hypotension decreased as personnel became more familiar with the potency of the drug.

Cardiac arrhythmias in this series have not been more serious in nature and have been less frequent in incidence than those seen with cyclopropane. They can be checked quickly by lightening the plane of anaesthesia. At the present time it is believed that epinephrine should not be injected when Fluothane is being employed.

The contraindications or limitations to the use of Fluothane have been falling by the wayside with regularity. Because of its potency, it has not been utilized in infants under six months of age. The potential hypotensive action has prevented its use in patients suffering from shock or in those with minimal cardiac reserve, such as patients coming to operation for mitral commissurotomy. It has been avoided in patients with grossly disturbed cardiac rhythm such as auricular fibrillation. Otherwise it is believed that Fluothane can be administered with relative safety. That safety is enhanced by an accurate method of vaporization and a careful, watchful anaesthesiologist at the head of the table.

#### ACKNOWLEDGMENTS

We wish to express our appreciation and thanks to our residents for their eager interest and to Mrs. Helen Parks for laboratory work.

## RÉSUMÉ

Le Fluothane,  $\text{CF}_3\text{CHClBr}$ , est un agent anesthésique par inhalation; il est puissant, non explosif et non inflammable, à l'Université Duke, nous l'avons administré à 500 malades pour en étudier les effets. Toutes sortes d'opérations ont été pratiquées chez des malades dont l'âge variait de 8 mois à 73 ans. Nous avons prescrit une prémédication ordinaire en surveillant toutefois que des doses adéquates de médicaments anticholinergiques soient administrées pour prévenir la bradycardie durant l'anesthésie

Chez 27 enfants, nous avons fait l'induction en employant la technique du goutte à goutte. Chez le plus grand nombre des malades, nous avons fait l'induction en administrant une dose anesthésique de thiobarbiturate, puis nous avons continué en employant, en circuit semi-fermé, du protoxyde d'azote 2 litres, de l'oxygène 2 litres pour vaporiser le Fluothane. Nous avons employé différents vaporisateurs dont la plupart avaient été jaugés antérieurement. Pour l'induction, il a fallu employer des concentrations de 2 à 4 volumes pour cent. Pour le maintien de l'anesthésie, nous avons employé la même technique, mais des concentrations de 0.5 à 1.5 volumes pour cent. De cette façon, nous avons obtenu un certain degré de paralysie musculaire, mais, au cours des opérations sur la partie haute de l'abdomen, nous avons dû employer un paralysant musculaire, la succinylcholine, nous l'avons employée également dans la chirurgie thoracique pendant les explorations hilaires pour prévenir les réactions sur le tube endotrachéal.

Le Fluothane permet une induction rapide de l'anesthésie, sans sécrétions salivaires, il calme précocement les réflexes pharyngés et laryngés et, aux plans d'anesthésie chirurgicale, il procure un certain degré de relâchement musculaire; il permet un contrôle facile de la profondeur de l'anesthésie, le réveil est rapide et s'accompagne d'un minimum de nausées et de vomissements.

Quand l'anesthésie est aux plans chirurgicaux, le centre respiratoire est déprimé au point que, chez presque tous les malades, il faut assister la respiration. Cette propriété ne doit pas être un inconvénient pour l'anesthésiologiste

Plus particulièrement au cours de l'induction, nous avons observé de l'hypotension qui a dépassé 20 mm. Hg chez 41 pour cent des malades. Chez tous les malades, à l'exception de 16, la pression sanguine est revenue à la normale sans que nous ayons dû recourir à une thérapeutique spéciale. L'incidence de l'hypotension a diminué à mesure que le personnel est devenu plus familier avec le pouvoir du médicament.

En employant les composés halogénés, il faut porter une attention spéciale aux manifestations hépatotoxiques. Au cours de cette épreuve, les tests de glycémie et le bromesulphaléine n'ont pas donné de résultats différents des cas témoins.

La sécurité de l'administration du Fluothane tient à la reconnaissance de sa puissance anesthésique. Dans le moment, l'appareil à notre disposition aux Etats-Unis ne nous donne pas assez de précision pour l'administration des faibles concentrations nécessaires. Il faudrait avoir des vaporisateurs nouveaux ou

modifier ceux que nous avons dans le moment. Nous avons la conviction que le Fluothane va avoir sa place comme anesthésique.

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