CLINICAL EXPERIENCE WITH FLUOTHANE®, A NEW NON-EXPLOSIVE ANAESTHETIC AGENT*

JONE CHANG, M D., F R C.P.(C), HUGH H. MACARTNEY, M.B., CH.B., and HORACE B. GRAVES, M.D.†

FOR MANY YEARS anaesthetists have felt the need for a non-explosive anaesthetic agent possessing none of the disadvantages associated with chloroform, trichlorethylene and nitrous oxide. That is, the agent should be non-hepatotoxic, stable in the presence of soda lime and heat, and have a high therapeutic ratio.

Since most heavily fluorinated hydrocarbons are not inflammable, and many possess anaesthetic properties, they present interesting possibilities. Robbins (1) found that some hydrocarbons had greater therapeutic ratios than chloroform or ether, but that when they were used, severe hypotension, cardiac arrhythmias and stimulation of skeletal muscle occurred.

In 1956, Raventós and Suckling synthesized and investigated a series of fluorinated hydrocarbons, and one in particular—CF_3 CHClBr (Fluothane)—was found to have potent anaesthetic properties (2). The first clinical trial has been reported by Johnstone (3) who studied the human cardiovascular response to Fluothane®.

PHYSICAL PROPERTIES

Fluothane® is a clear colourless liquid with a rather pleasant odour. It has a specific gravity of 1 86 at 20° C. and a boiling point of 50.2° C. Vapour pressure at 20° C. is 243 mm. Hg. Oil/water solubility is 330 compared to 100 for chloroform and 3,2 for ether. When exposed to light, Fluothane decomposes slowly, forming volatile acids. This can be prevented by storing it in amber-coloured bottles or by adding thymol 0.01 per cent W/W. Fluothane is non-inflammable, non-explosive and stable in the presence of soda lime.

Fluothane should not be confused with Fluomar® (trifluoro-ethyl-vinyl ether), an inflammable fluorinated ether with somewhat different properties, described by Orth (4) and Gainza, *et al.* (5).

PHARMACOLOGY

Raventós (2) investigated the pharmacological actions of Fluothane in animals and reported that full surgical anaesthesia was achieved after using a 2–4 per cent concentration of Fluothane in air or oxygen for two to five minutes.

Anaesthesia was maintained with a concentration of 0.4–0.8 per cent in premedicated dogs, and 1–1.2 per cent in unpremedicated ones. On the basis of

*Fluothane® was supplied by Ayerst, McKenna & Harrison Limited, Montreal, Canada.

†Department of Anesthesiology, Vancouver General Hospital and University of British Columbia, Vancouver 9, British Columbia.

Presented at the Annual Meeting of the Canadian Anaesthetists' Society, Saskatoon, Saskatchewan, June 24–26, 1957.

these findings Fluothane would seem to have double the potency of chloroform and four times that of ether.

Respiration was decreased in amplitude and rate, but especially in rate. When administration was continued to respiratory arrest, blood pressure was still 60–80 mm. Hg, and the heart continued to beat for nine to ten minutes.

Blood pressure fell in proportion to the vapour concentration and the fall was most marked during induction.

Heart rate was consistently slowed, but no irregularities were noted except in the presence of epinephrine and norepinephrine, when ventricular tachycardia and ventricular fibrillation were produced.

Salivation and mucous secretions were abolished, and vomiting did not occur at any time. No significant functional or histological changes were found in liver or kidneys in animals, after prolonged Fluothane anaesthesia.

In view of the interesting properties of Fluothane, it was felt that a trial should be made with a wide variety of cases to assess its suitability for clinical use

The series was divided into two parts—Series I and II In Series I, Fluothane was used in a closed circuit soda lime absorption system, for the most part using Fluothane for induction also (H H M) In Series II, Fluothane was used in the semi-closed system, following thiopentone induction (J.C.).

SERIES I USE OF FLUOTHANE IN THE CLOSED CIRCUIT

Selection of Cases

The series consisted of 120 consecutive cases assigned to the particular operating room in which the author was working Only young children were excluded as it was felt that the use of an experimental agent with a closed circuit in these cases was potentially hazardous.

Age of Patients

Ages ranged from 17–84 years, with approximately an even number in each decade between 20 and 80.

Types of Surgical Procedures

Duration of surgery ranged from 15 minutes to 4½ hours with the majority of the cases lasting 2 hours and under.

Anaesthetic Equipment

The ether vaporizers on the Foregger, Heidbrink, McKesson and Chicago Anaesthetic machines were used, concentration of Fluothane being judged on purely clinical observations.

Those vaporizers employing a wick appeared to be the most satisfactory.

METHOD

Premedication This was standardized as far as possible with the average male receiving a short-acting oral barbiturate, gr 1½, two hours preoperatively,

followed by morphine, gr. ¼, and hyoscine, gr. 1/100, one hour preoperatively These dosages were reduced for small females, the severely ill and the aged

In 33 cases intravenous atropine gr. 1/200–1/50 was given 10 minutes prior to induction. The effect of this will be discussed below.

Prior to induction, blood pressure, respiratory and pulse rate were recorded. In 21 cases simultaneous respiratory rate, minute and tidal volumes were measured, using a Monaghan ventilation meter.

Type	*Number*	*Type*	*Number*
General surgery		Plastic surgery	6
Major	23	Orthopaedic surgery	
Minor	15	Major	4
Gynaecological surgery		Minor	1
Major	14	Thoracic surgery	4
Minor	19	Genito-urinary surgery	
Abdominal surgery	21	Major	2
Vascular surgery	10	Minor	1

Induction. Intravenous thiopentone was used to induce 24 patients, while the remaining 96 were induced with Fluothane by mask. The technique was as follows:

The patient was first asked to breathe a mixture of N_2O and O_2, 4 and 2 litres per minute respectively When the patient was lightly asleep, Fluothane was gradually turned into the circuit and the N_2O turned off (Although Fluothane/O_2 induction was not unpleasant, preliminary N_2O induction proved to be more agreeable to the majority of patients)

After about 10 minutes of Fluothane, the vaporizer setting had generally reached the three-quarter mark and blood pressure had fallen to about 60 mm Hg By this time sufficient anaesthesia was usually present for surgery, so the O_2 was turned down to basal requirements and the circuit closed Fluothane now was either turned off or turned back to the lowest setting About 10 minutes prior to completion of surgery, the Fluothane was turned off completely and a 4/2 litre per minute flow of N_2O/O_2 started, in order to eliminate as much Fluothane as possible

During the procedure blood pressure, pulse and respiration rates were recorded at 5-minute intervals, as well as frequent minute and tidal respiratory volumes for 21 patients.

Where indicated, intubation was performed following a relaxant, the other patients being carried with a mask.

Results

With adequate premedication, Fluothane induction was moderately rapid and smooth, free from coughing, laryngospasm, or salivation. With light premedication, induction tended to be slower and was often marked by violent struggling with a period of generalized muscle rigidity During this period masseter spasm often prevented insertion of an oral airway.

After ten minutes the muscle rigidity gave way to relaxation and after fifteen minutes, surgery could be commenced, although reflex movement was occasionally observed. This was associated with a rise in blood pressure and tachypnoea.

After 20–25 minutes, reflex movement was abolished, though abdominal relaxation was insufficient for upper abdominal exploration. At this time intubation

could be performed without the need for a relaxant, the cords, being widely abducted.

Cardiovascular System

Effect on Blood Pressure (Table I)

Within the first few minutes of Fluothane induction, pulse rate and blood pressure declined progressively, systolic fall being relatively greater than diastolic, resulting in a low pulse pressure. Fall in blood pressure appeared to be directly related to the concentration of Fluothane and especially to the rapidity with which concentration was increased. The average fall in pressure during Fluothane induction (taken as the first 30-minute period) was 42 mm. Hg.

TABLE I

Degree of Hypotension during Induction

B P drop mm Hg	Number of cases		
	Total series	Series without pre-induction I V atropine	Series with pre-induction I V atropine
Nil	6	4	2
–20	37	22	15
21–40	37	29	8
41–60	18	14	4
61–80	10	8	2
81–100	7	6	1
110–120	1	1	0
121–140	3	2	1
141–160	1	1	0
Total	120	87	33
Average B P drop mm Hg	40	43	31

Average Fluothane® induction B P fall, 42 mm Hg
Average Pentothal/Fluothane® induction B P fall, 46 mm Hg

After the initial fall and when the vaporizer setting was decreased, blood pressure usually rose to around 80 mm. Hg and fluctuated on either side of this level, depending on the setting of the vaporizer.

Effect of Atropine on Induction Hypotension (Table I)

Atropine gr. 1/200–1/50 was given to 33 patients intravenously 10 minutes prior to induction, to see if preventing bradycardia could affect the fall in blood pressure. Within a few minutes of injection, blood pressure rose on the average 20 mm. Hg and pulse rate increased to about 120 per minute. Following induction, blood pressure declined as in the non-atropinized patients, though to a lesser extent.

The average fall in the atropinized patients was 31 mm. Hg. During maintenance, average blood pressures in these patients were about 10 mm. Hg higher than in non-atropinized patients. In fact, in many patients who were given

atropine, systolic blood pressure and pulse rate were frequently numerically equal, while in the non-atropinized ones pulse rate and diastolic blood pressure were often equal, or nearly so.

Effect of Age on Induction Hypotension

In the entire series there were 37 patients, 60 years of age or over. The average fall in blood pressure for them was 44 mm. Hg compared with 45 mm. Hg for the patients under 60 years of age.

In the eleven patients 60 years of age and over who were given intravenous atropine prior to induction, the average fall was only 27 mm. Hg, while the remaining 26 who received no atropine had an average fall of 51 mm. Hg.

Although the number of patients in each group is relatively small, it would appear that only in the older age groups was any significant benefit derived from pre-induction atropine.

Degree of Induction Hypotension

All degrees of hypotension were seen, from no perceptible decrease to complete absence of recordable blood pressure or pulse, the latter occurring in twelve patients (10 per cent). In Table II, the degree of hypotension sustained is shown. As can be seen, there is no very significant protection afforded by atropine in the over-all series.

Severe Hypotension Episodes

In the twelve patients referred to above, blood pressure and palpable radial and carotid pulsation disappeared following attempts to deepen the anaesthesia. It appeared as if cardiac standstill had occurred in each case, the only hopeful signs of continuing circulation being the fact that the skin remained pink and warm, and a faint capillary refill was present.

Except for one case which will be described in detail below, inflation of the lungs with 100 per cent oxygen rapidly restored blood pressure and pulse within a minute. This was found to be the most reliable treatment, as neither vasopressors nor atropine at this time were very effective, since circulation was sluggish. Less profound hypotension responded better to Methedrine® than to Neosynephrine®, the latter commonly causing frequent extrasystoles

Since blood pressure returned so rapidly, it was felt that the sudden hypotension was mainly due to sudden increase in concentration of Fluothane, causing myocardial depression.

After analysing the twelve cases, it was seen that in every one concentration had been increased just prior to the episode, and except for two cases, followed manual ventilation after the use of a relaxant. Succinylcholine was the relaxant in seven, C_{10} in one, and gallamine in two cases.

Except for one instance, all episodes occurred within the first 30 minutes following induction. Of the twelve patients, five had intravenous atropine before induction, which conferred no protection against hypotension of this sort.

No relaxant was given to two patients prior to the hypotensive episode, but thiopentone in small doses was given in addition to increasing Fluothane® concentration.

Cardiac Arrest

One cardiac arrest occurred in the entire series, though fortunately without fatal result.

Case report A 38-year-old white male was to undergo a transthoracic vagotomy for treatment of a chronic stomal ulcer Preoperative examination showed an otherwise healthy 155-lb. man, B P 120/80, pulse 72/minute.

Premedication consisted of morphine gr 1/6 and hyoscine 1/100 gr, given 1 hour preoperatively.

The patient was induced at 11 00 A M with thiopentone 500 mg and intubated following decamethonium 3 mg with a cuffed # 9 O T tube He was maintained on Fluothane/O_2 in a closed circuit and was postured in the right lateral position with the table flexed.

Following the induction and positioning of the patient, blood pressure gradually declined as expected with Fluothane, and at 11 25 A M, blood pressure was 80/60 mm. Hg and pulse 60/minute Atropine gr 1/100 was given intravenously in order to correct the hypotension.

As the surgeon made the skin incision the patient began to shiver violently and made movements as if reacting to the stimulus As it appeared the patient was in a light plane of anaesthesia, thiopentone 125 mg was given and the Fluothane vaporizer setting increased, ventilation all this time being controlled

At 11 35 A M, blood pressure and pulse, which had been carefully watched, suddenly disappeared and Methedrine® 20 mg was given intravenously, together with inflation with 100 per cent O_2 with the Fluothane turned off

The face now appeared slightly cyanosed and bleeding in the wound ceased The surgeon was advised that a cardiac arrest was probable and the thoracotomy was rapidly completed

On opening the chest cavity, the heart was seen to be in standstill but still pink, and immediate manual compression was performed After 4 compressions the heart restarted, blood pressure could be just obtained at 45 mm Hg, and the surgeon observed that the heart when first palpated was flabby Suddenly ventricular fibrillation commenced and heart was compressed for a further minute, till the electrical defibrillator could be set up

After 4 separate shocks of 220 v. at 0 2 sec, defibrillation was successful Following a few seconds of asystole, the heart began to beat rapidly and irregularly, blood pressure rising to 180/140 mm. Hg, presumably in part owing to the Methedrine®. The pericardium was not opened

The surgery was completed at 1 30 P M and by that time blood pressure was 120/80 mm. Hg and pulse 100/minute

The patient was transferred to the recovery room, and by 1 45 P M., was reacting, and at 2 00 P M was conscious E C G taken at this time was completely normal

The patient made a speedy recovery from the surgery and showed no evidence whatsoever of cerebral damage He was discharged after 10 days and resumed work shortly after

It was estimated that circulation had been arrested for a period of 1 to 1½ minutes

Blood Pressure during Maintenance

Using Fluothane in the closed circuit it was rarely possible to maintain a steady blood pressure level, as small changes in the vaporizer setting caused almost immediate alteration

Degree of myocardial depression and depth of anaesthesia did not seem necessarily related, as blood pressure, especially in the induction period, could be quite low and yet there was reaction to surgical stimulus, as illustrated in the case described above where cardiac arrest occurred.

After several hours a smooth level appeared to be easier to maintain, possibly because of decreased blood/tissue gradients

Effect on Pulse Rate and Rhythm

Rate. During induction pulse rate slowed with decline in blood pressure. In the majority of patients pulse fell to 60 per minute and remained about that level until anaethesia was lightened, when it rose to around 70 per minute. Rates as low as 40 per minute have been noted, and with the use of intravenous atropine may run from 80–120 per minute with similar systolic blood pressure.

Rhythm. Fluothane caused pulse irregularities in seventeen patients. These took the form of irregularly spaced extrasystoles, showing as occasional weak beats, and a peculiar bigeminal rhythm with a pulsus alternans character. These were diagnosed by palpation of the radial pulse and noted alteration in blood pressure level.

There appeared to be a zone of anaesthesia in which arrhythmias occurred, as deepening or lightening the anaesthesia, especially the latter, often caused the pulse to become regular.

Two cases, in which atropine was given intravenously, immediately converted to a faster regular rhythm. In five cases with bigeminal rhythm, atropine had been given intravenously just before induction, so did not appear to have had any prophylactic value.

No particular age group was immune or especially susceptible to arrythmias, these being seen in patients aged from 20–82 years.

Bleeding. This was greatly diminished, possibly owing to decreased pulse pressure and in part to a relative hypotension. However, bleeding was also minimal even where blood pressure was still close to the preoperative level. The diminution in bleeding was one of the most remarkable properties of Fluothane and affected all but the larger arterioles which still bled normally.

Postoperative haemorrhage of the wound occurred in two patients, but appeared to be due to a slipped ligature in each case.

Venous system. Early in induction the veins became very prominent and even tense, suggesting a raised venous pressure, possibly due to a decreased cardiac output

Postoperative blood pressure Blood pressure readings were taken immediately on the patient's return to the recovery room and show the following results:

Higher blood pressure than preoperative level, 27 per cent
Same blood pressure as preoperatively, 22 per cent
Blood pressure drop of not more than 20 mm below preoperative level, 31 per cent
Blood pressure 21–40 mm Hg below preoperative level, most of which were readily corrected by elevating the foot of the bed, 10 per cent (2 cases responded promptly and permanently to Methedrine®)
Fall below 40 per cent, 0
Immediate postoperative blood pressures not recorded, 10 per cent

Respiratory System

In 21 cases minute volumes, tidal volumes and respiratory rates were correlated using a Monaghan Ventilation Meter. As can be seen from Table II, most patients had some degree of respiratory depression on arrival in the operating

suite due to preoperative sedation. Depression was proportionately greater in women than men.

TABLE II

PREOPERATIVE VENTILATION

Age	Weight (lb)	Minute volume (litres)	Tidal volume (cc)	Rate
MALES				
68	–	8 6	610	14
54	–	6 0	500	12
26	138	5 2	300	17
66	165	4 8	260	18
48	145	4 8	260	18
74	–	4 2	300	14
50	–	4 0	330	12
75	–	4 0	330	12
66	168	3 3	470	7
FEMALES				
43	160	8 0	500	16
41	–	6 0	500	12
37	181	4 0	220	18
60	–	3 6	360	10
37	130	3 2	320	10
66	–	3 0	165	18
25	–	2 6	160	16
46	118	2 6	260	10
65	160	2 2	200	11
50	120	2 0	100	20

As illustrated in Figures 1, 2 and 3, during induction there was a progressive increase in respiratory rate, associated first with a transient increase in tidal and minute volumes as unconsciousness occurred This rapidly changed to faster and shallower breathing, causing a progressive decrease in tidal and minute volumes when anaesthesia became light With surgical stimulus respiration became very fast—up to 40 per minute and was associated with larger tidal volumes, resulting in large minute volumes—up to 12 litres per minute.

When anaesthesia was deepened, respiratory rates usually increased and respirations became very shallow, with sharp decreases in tidal and minute volumes Progressive deepening of anaesthesia finally led to complete apnoea, though blood pressure was still usually around 70 mm Hg

Thus, it seemed that spontaneous respiration was a safety factor, as precipitous blood pressure drops to zero only occurred when controlled respiration with a high vaporizer setting was employed.

It was found very easy to take over control of the respiration without the need of relaxants, and when it was desired the patient would also resume control within a very short time

At the termination of surgery, when the Fluothane was being blown off with a high flow of N_2O/O_2, respiration always slowed and deepened, with resumption of normal minute volumes

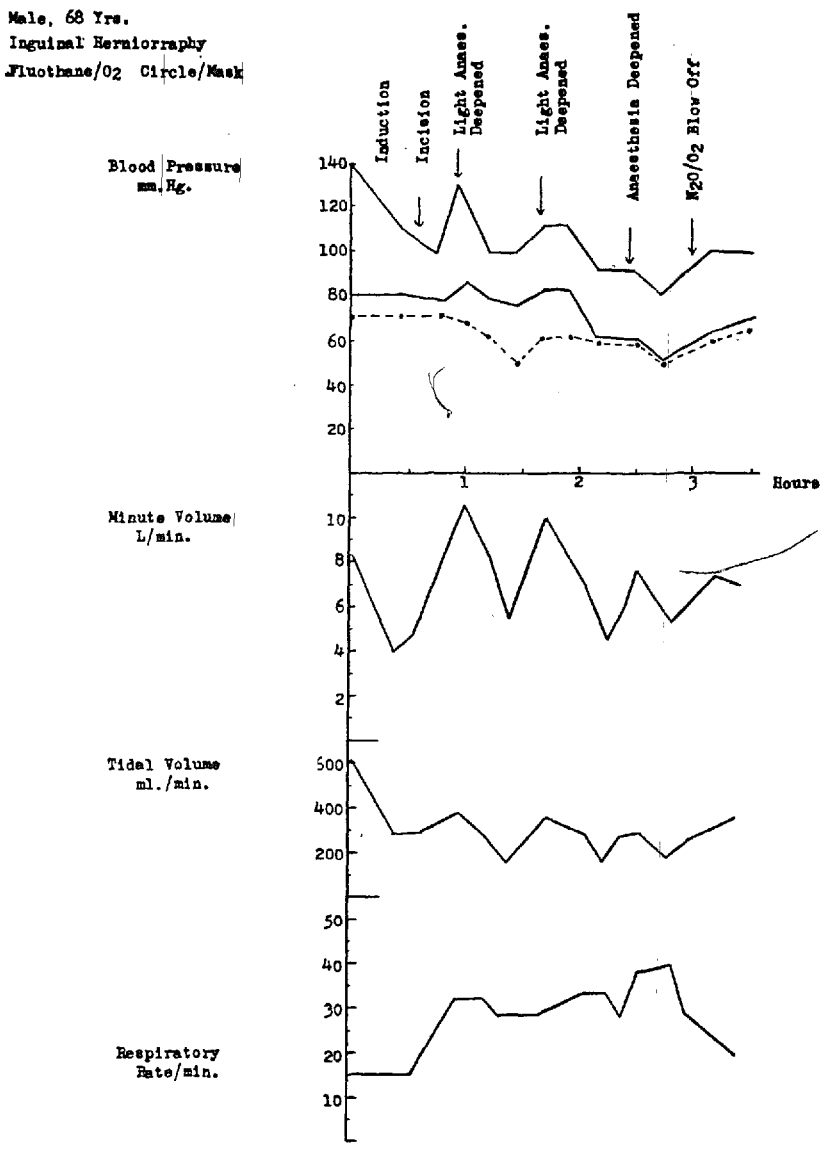

FIGURE 1

Fluothane in asthma. One patient had audible bronchospasm preoperatively. After five minutes of Fluothane the bronchospasm disappeared and did not return until several hours postoperatively.

Bronchial secretion. Markedly diminished, though several patients appeared to cough up tenacious sputum for several days postoperatively.

Muscular System

During induction there was frequently a transient period of generalized muscle rigidity which gradually relaxed.

In general, muscle relaxation was only fair to moderate, and attempts to increase it were limited by hypotension. Most lower abdominal incisions could be closed without relaxants, but upper abdominal incisions generally required a relaxant. However, it was noted that after about three hours of Fluothane administration, relaxation improved and often was equal to that seen in spinal

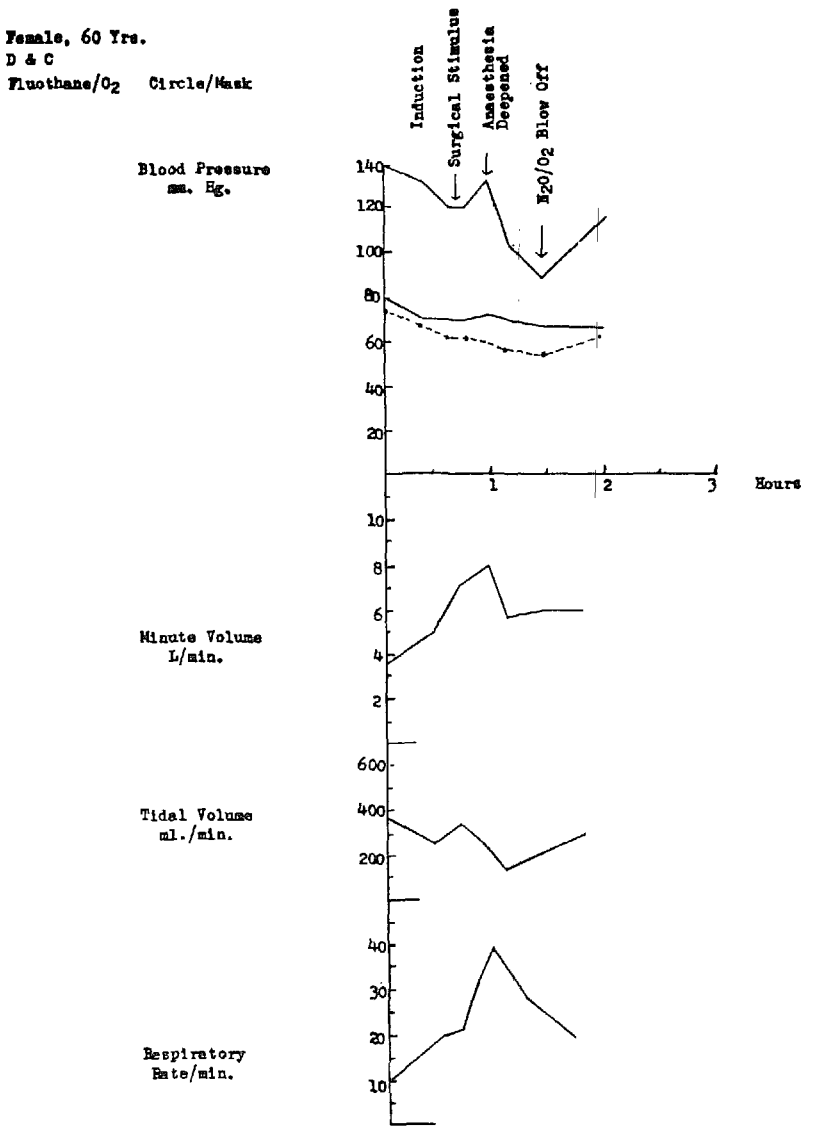

FIGURE 2

anaesthesia. In these cases respiration was controlled, which may have added to the effect.

On emergence a not infrequent phenomenon was a short period of muscle rigidity in the form of intense shivering. In several patients it was extremely violent and the patient's respiratory muscle spasm temporarily caused complete apnoea.

Effect of Muscle Relaxants

Succinylcholine and C_{10} acted in their usual brief fashion, but d-tubo curare and gallamine usually had relatively brief actions lasting on the average only ten minutes. On many patients 60 mgm. doses of gallamine produced no perceptible effect. Consequently, patients requiring continuous relaxation needed large total dosages of these two drugs.

No hypotension was noted which was directly attributable to the use of d-tubo curare and Fluothane, as reported by Johnstone. Seven patients were given

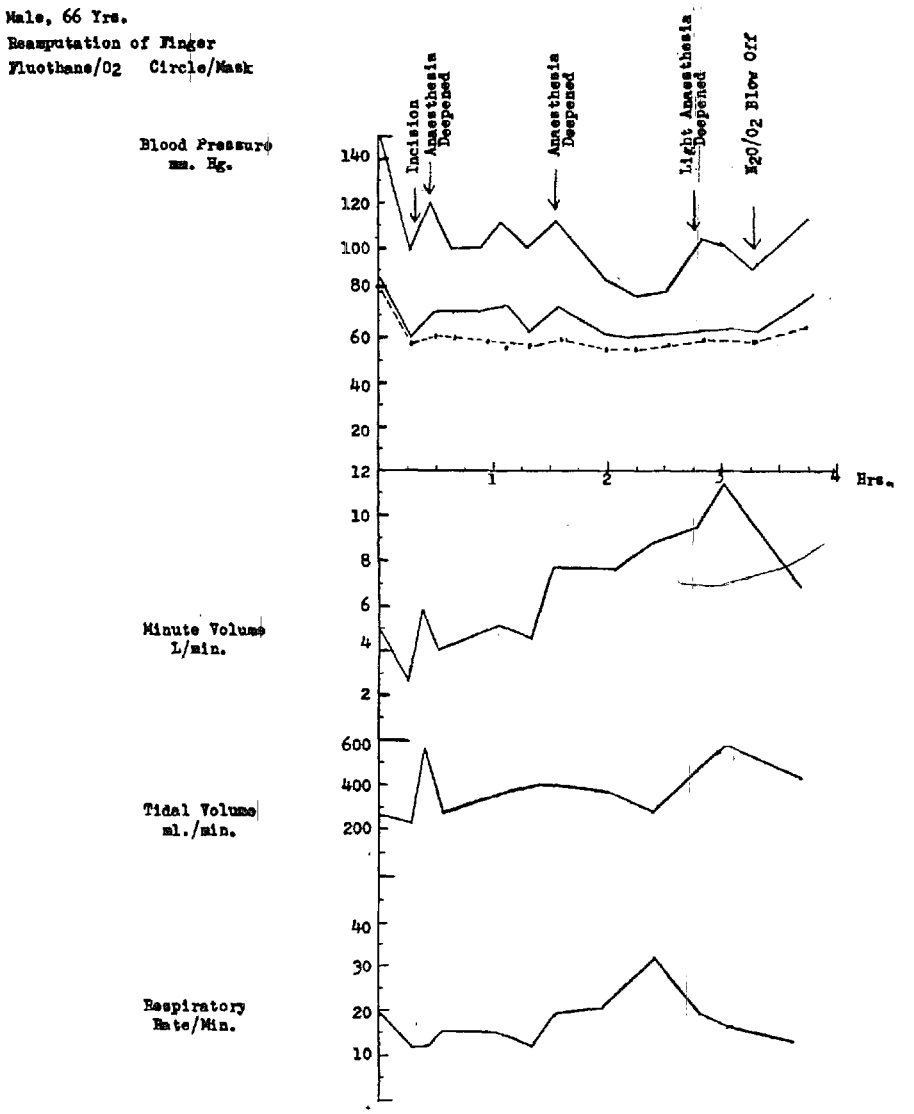

FIGURE 3

d-tubo curare in total dosages ranging from 9 mg. to 27 mg. without any blood pressure change whatsoever.

SKIN

In all patients the skin became warm, dry and pink as it does following spinal anaesthesia.

ALIMENTARY CANAL

During most abdominal procedures the gut appeared to be constricted during administration of Fluothane.

VOMITING

The multitude of factors associated with anaesthesia and surgery make the exact cause of postoperative vomiting difficult to assign. However, it is probable

that most vomiting due to the anaesthetic occurs within the first few hours after operation.

We have arbitrarily divided the postoperative period into two groups. one up to four hours postoperatively, the other within the first 24 hours postoperatively Of the 120 patients, 4 vomited within the first 4-hour period, giving an incidence of 3.3 per cent, 14 patients vomited at some time within the first 24 hours, giving an incidence of 8 5 per cent. (Since many of these patients had intra-abdominal procedures and received opiates it would be unfair to attribute all vomiting to the anaesthetic.)

Salivary and Mucous Secretions

Several patients were induced with Fluothane without previous atropine or hyoscine and no increase in secretions was noted. In fact, in many cases belladonna drugs may be unnecessary. This effect was of particular help in thoracic surgery.

Recovery from Anaesthesia

Raventós (2) reported recovery time from Fluothane in animals to be 10 to 20 minutes, even after 5 to 6 hours of anaesthesia. Johnstone (3) likewise described patients being rousable some 10 minutes after discontinuing Fluothane.

The time at which the patients first reacted, as well as the time when they were fully conscious, was recorded by the recovery room staff (Tables III, IV). The latter were totally unaware that any series of cases was being studied and so their observations were not influenced in any way

TABLE III

Time until Reacting Postoperatively

Time until reacting postoperatively (minutes)	Duration of surgery in hours				
	0–1	1–2	2–3	3–4	4–5
Under 15	6	2	2	1	–
15	10	7	6	2	2
30	4	5	3	2	1
45	3	1	3	–	1
60	–	1	1	1	–
75	–	3	–	–	–
90	–	–	2	–	1
105	–	–	–	–	–
120	–	1	–	–	–

From Table III it is seen that of the 71 cases studied for reacting time, the majority were reacting within the first 30 to 45 minutes postoperatively, and were conscious in an average of 60 minutes after completion of surgery (Table IV) It can be seen that increasing duration of anaesthesia was associated with in-

TABLE IV

TIME UNTIL CONSCIOUS POSTOPERATIVELY

Recovery time (hours)	(minutes)	Duration of surgery in hours 0–1	1–2	2–3	3–4	4–5
	5	1	–	1	–	–
	15	11	3	2	1	–
	30	10	10	4	4	–
	45	4	7	1	2	1
1		5	6	6	1	3
1	15	3	2	3	1	–
1	30	–	5	2	2	–
1	45	–	1	–	–	–
2		1	3	4	–	–
2	15	–	–	–	–	–
2	30	–	3	–	–	–
2	45	–	–	1	–	–
3		2	–	–	–	1
Over 3		1	–	–	1	1
Number of cases		38	40	24	12	6
Average time in minutes		50	60	65	65	105

creasing recovery time, though the difference between the groups was most marked in the procedures lasting four to five hours.

CONTROLLED HYPOTENSION WITH FLUOTHANE

Although generally speaking bleeding from small vessels was minimal with Fluothane anaesthesia despite normal or near normal pressures, it was further minimized for plastic and other operations with satisfactory results.

It proved to be easier to maintain the blood pressure evenly at 65 or 70 mm. Hg than at 100 mm Hg. For this reason and also because blood pressure can be so readily raised, Fluothane was frequently requested when minimal bleeding was required.

DEATHS

There was only one death in the series occurring within one month of operation. This was an 84-year-old male who had a subtotal gastrectomy for a carcinoma of stomach. He died 26 days postoperatively, and autopsy revealed pulmonary infarction, pulmonary abscess and a terminal pneumonia.

No connection could be found between his death and the anaesthetic procedure.

SERIES II USE OF FLUOTHANE IN THE SEMI-CLOSED SYSTEM

METHOD

In this series of cases Fluothane was administered to 190 patients. The patients were premedicated with the usual agents—morphine or Demerol, together

with a belladonna drug, with the exception of craniotomies, where belladonna drugs alone were given. In few cases phenergan or barbiturates were added to the premedication. Pentothal® in doses of 100 to 500 mgm.—average 200 to 250 mgm.—was routinely injected for induction. When endotracheal technique was indicated, succinylcholine was administered in doses of 60 to 100 mgm. to facilitate intubation. All the patients were maintained on a semi-closed system with a 10-litre flow of gas, either oxygen or oxygen and nitrous oxide in 50-50 concentration. Most of the patients were allowed to breathe spontaneously with little or no assistance to respiration. The age group of these patients ranged from 6 days to 83 years.

Types of Cases

Neurosurgical	67	36.2%	Urological	14	7.6%
Laparotomies	20	10.4%	Thoracic	7	3.6%
General surgical	31	16.0%	Orthopaedic	9	4.6%
Gynaecological	32	16.6%	Plastic	6	3.1%
		Endoscopic 4 2.1%			

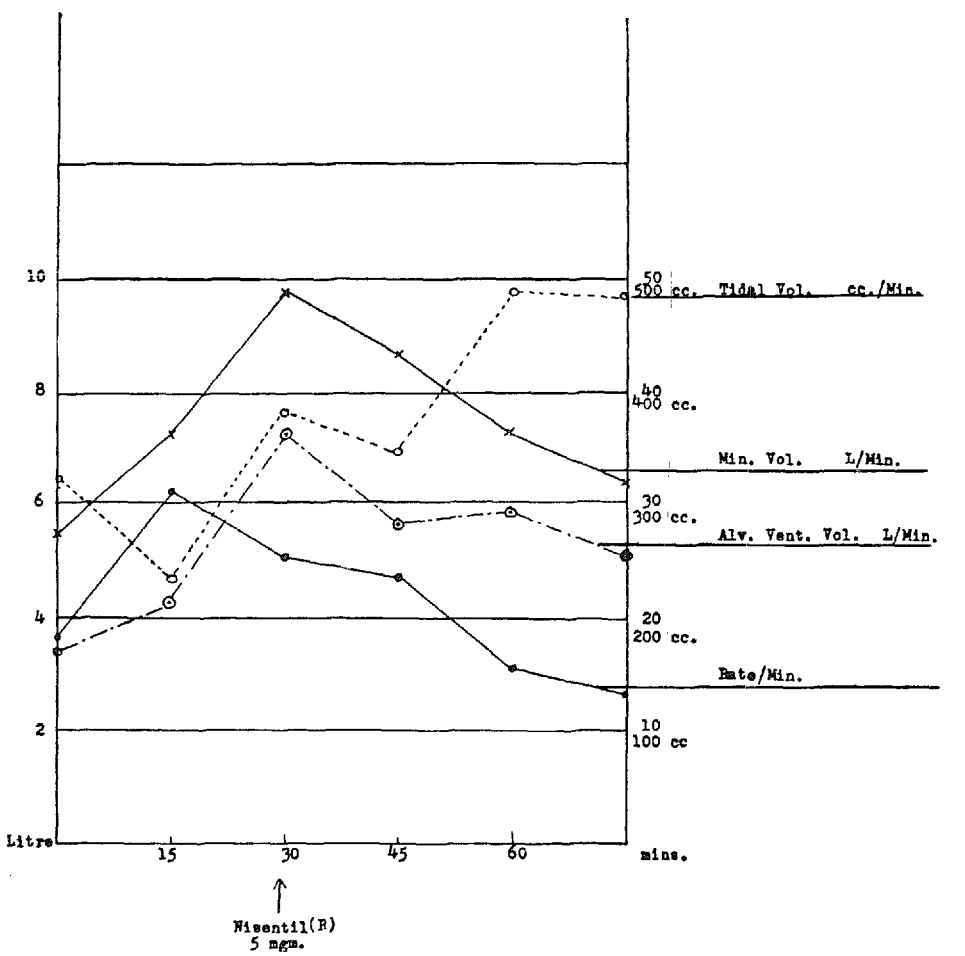

Figure 4

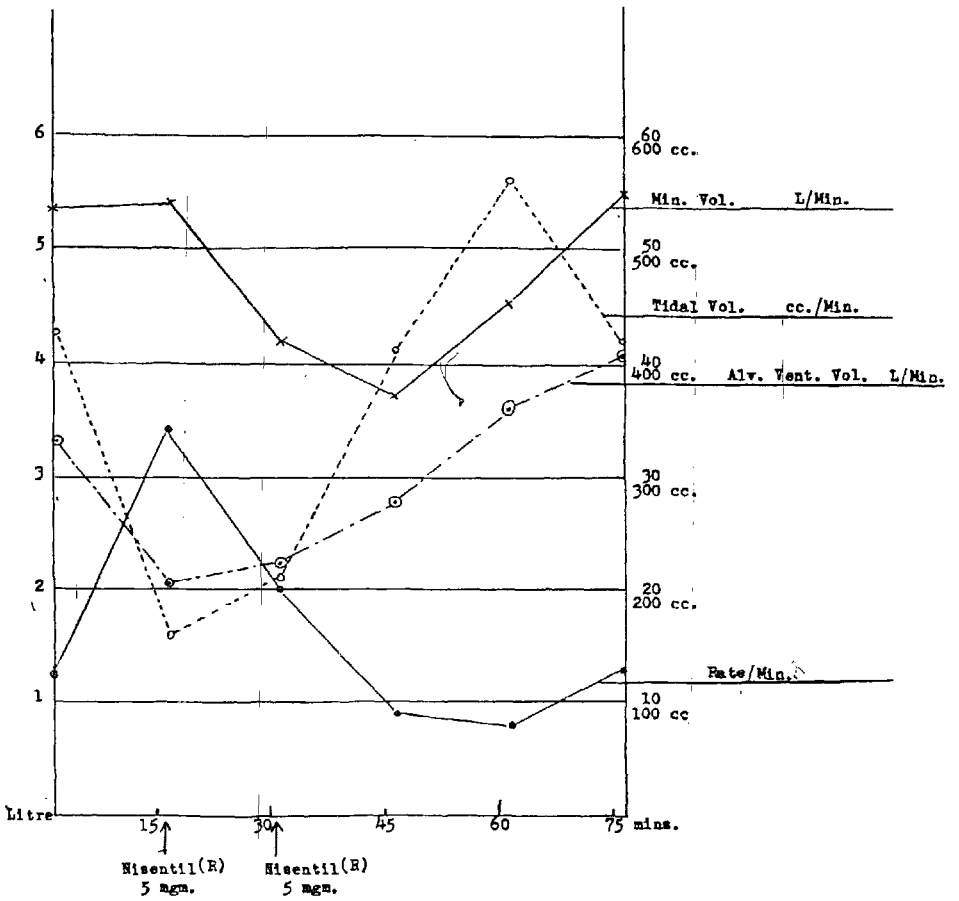

FIGURE 5

RESULTS

Induction was usually carried out rapidly with Pentothal®, and Fluothane was added slowly to the semi-closed circuit. Fluothane caused little excitement during the induction period. Adequate surgical anaesthesia was usually established in about five minutes. There was little or no laryngospasm or bronchospasm with increasing concentration of the agent.

RESPIRATORY SYSTEM

Fluothane had a marked effect on the respiratory function under anaesthesia. In practically all the cases the rate of respiration was increased to a greater or lesser extent. Respiratory rates as high as 50 per minute were noted. The tidal volume fell in an inverse relation to the rate: that is, as the rate of respiration increased the respiration became shallower. If the rates of respiration were decreased by the use of an opiate, the respiration became deeper. In this series of cases Nisentil in doses of 5 to 15 mgm. was given either intravenously or intramuscularly to reduce the tachypnoea during anaesthesia. These changes are illustrated by the accompanying graphs (Figs. 4, 5 and 6). During anaesthesia there was no stimulation of secretion in the respiratory tract. The respiration during anaesthesia appeared to be adequate in patients with spontaneous respira-

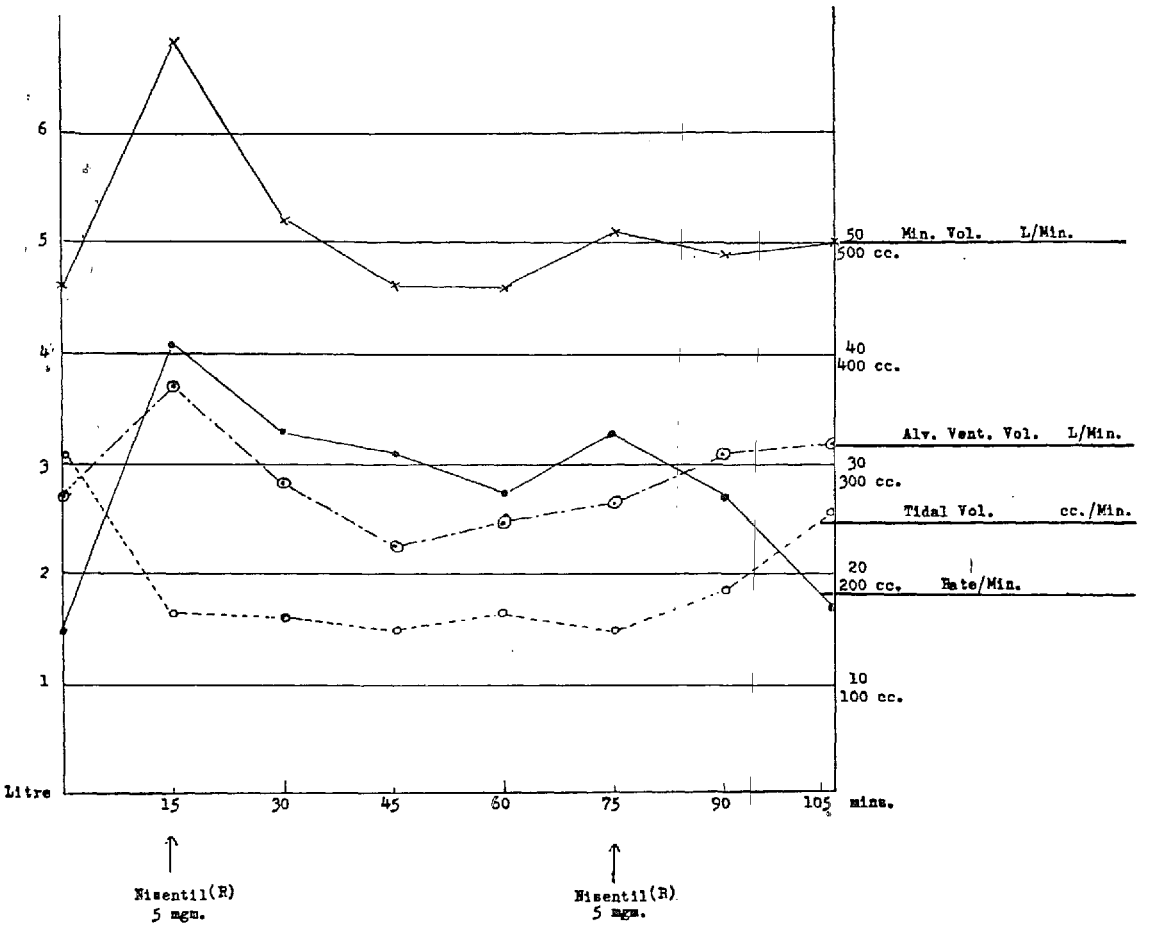

FIGURE 6

tion. The minute volume was slightly increased or decreased as illustrated, while the tidal volume varied inversely with the rate. In most of the cases endotracheal technique was used so that the dead space was reduced by at least one-third; thus efficient respiration could be maintained with a smaller minute and tidal volume.

CARDIOVASCULAR SYSTEM

The cardiovascular effect of Fluothane appeared to be the major limiting factor of the agent. A rapid increase in concentration of the vapour, or deep anaesthesia, decreased the blood pressure. The blood pressure could be decreased very rapidly and there were two cases where rapid increase in concentration dropped the blood pressure to unrecordable levels. In most of the cases under surgical anaesthesia, the blood pressure was maintained with no marked fall.

B.P. fall during anaesthesia	*Per cent*	*Postoperative B.P.*	*Per cent*
Less than 20 mm. Hg	58	Above preoperative	43
21 to 40 mm. Hg	30	Less than 20 mm. Hg below	43
Over 40 mm. Hg	12	21 to 40 mm. Hg below	12.5
		Over 40 mm. Hg below	1.5

There was little depression of the blood pressure during the immediate post-operative period as shown by the above chart. The blood pressure changes could

be attributed to central action, as a ganglionic blocking agent still reduced the blood pressure with varying sensitivity, from very sensitive to relatively resistant. Arfonad was used to lower the blood pressure on five occasions with no difficulty. In a small series of seven thoracotomies, there appeared to be a greater difficulty in maintaining blood pressure. As a rule the blood pressure level settled to about 60 mm. Hg even under light Fluothane anaesthesia.

The occasional arrhythmias encountered were minor. Bradycardia was commonly found with Fluothane though in most instances it was not severe. Therefore, extra atropine prior to the induction of anaesthesia was not essential. With marked bradycardia atropine will reverse the slow rate.

Relaxation

Relaxation under Fluothane varied with the depth of anaesthesia. In lighter planes of anaesthesia the relaxation was only moderate. With spontaneous respiration, relaxation of the abdominal muscles was moderate, often requiring the aid of relaxant drugs to facilitate closure of the peritoneum. The masseter muscle was adequately relaxed for purposes of intubation.

Nausea and Vomiting

Nausea and vomiting is probably less than with the other agents In the immediate postoperative period—4 hours—only 8 per cent of the patients were nauseated or vomited, while in the first 24 hours, 13 7 per cent were nauseated or vomited

Recovery Time

As a general rule the recovery from an anaesthetic varies with the duration of the operation. Where Fluothane was used, the time of emergence from anaesthesia depended on the duration of anaesthesia. Where the procedure was less than one hour, the average time for regaining complete consciousness was 37 minutes, for cases between one and three hours, 70 minutes, and over three hours it was 90 minutes

Deaths

There were five postoperative deaths in this series. None of the deaths was related to anaesthesia. Two deaths followed craniotomy for brain tumour; one death was from a myocardial infarction eleven days after a Smith-Petersen nailing of the hip, one death from massive haemorrhage during a thoracotomy, and the final death followed a thoracotomy for advanced bronchogenic carcinoma.

Discussion

The non-irritant properties of Fluothane made induction with it reasonably pleasant, though being relatively slow it is less convenient than thiopentone induction.

However, in Series I, Fluothane induction served to demonstrate its true cardiovascular and respiratory effects.

The cardiovascular effects of Fluothane are mainly hypotension and bradycardia, associated with cutaneous vaso-dilatation. Venous dilatation occurs early, facilitating venepuncture.

The severity of the hypotension and bradycardia is directly proportional to the rate and magnitude of the increase in vapour concentration.

Induction hypotension was less marked using a semi-closed technique, with only 12 per cent of the patients having a systolic drop of more than 40 mm. Hg, compared to 33 per cent with the closed circuit.

Again it is noted that 10 per cent of the patients anaesthetized with the closed technique had blood pressure falls to unrecordable levels, as opposed to only 1 per cent anaesthetized with a semi-closed technique. With the latter technique, using a high gas flow, Fluothane concentration can be kept relatively constant, and it is probably the technique of choice.

Atropine, by causing a tachycardia, will tend to minimize the initial induction hypotension, but is probably of value mainly in the older age group. During maintenance, intravenous atropine is quite effective in raising blood pressure when it is low, the rise not being above preoperative levels. Thus the use of atropine may permit a deeper plane of anaesthesia to be reached, when depth would otherwise be limited by the hypotension.

One cardiac arrest occurred in the series, reminding us of the vigilance with which blood pressure levels must be watched.

The decrease in bleeding constitutes one of the most important properties of Fluothane, especially as it does not appear to depend on hypotension.

With Fluothane, controlled hypotension is easily obtained and can be reversed very rapidly. If desired, Arfonad may be used with Fluothane to produce controlled hypotension in a lighter plane of anaesthesia.

Arrhythmias are fairly common, mainly in the form of extrasystoles and bigeminal rhythm, but disappear readily when the anaesthesia is lightened or atropine is used.

Postoperatively blood pressure is well maintained and over 80 per cent of patients had blood pressures not less than 20 mm. Hg below preoperative levels. With the semi-closed and closed techniques, 27 per cent and 43 per cent, respectively, had blood pressures above the preoperative level

Respiration becomes rapid and shallow, though in the lighter planes it appears adequate, especially with the use of an endotracheal tube to reduce dead space. With deeper planes, the respiratory rate, though rapid, does not compensate for the decreased tidal volume, and thus minute volumes tend to be below normal. If respiratory rate is slowed with an opiate, the minute volume increases again owing to a greatly increased tidal volume. Thus, with respiratory rates of 30 per minute or over, respiration should either be assisted or slowed with an opiate.

In light planes of anaesthesia surgical stimulus causes a marked increase in respiratory rate and depth, resulting in large tidal and minute volumes. This respiratory change usually precedes reflex movement by the patient and allows anaesthesia to be deepened to prevent this.

As blood pressure is depressed early, anaesthesia may still be light even though hypotension has occurred, and at this time there may be the respiratory signs

of light anaesthesia. It is at this time that anaesthesia should be deepened with great caution.

The ease with which respiration can be controlled with Fluothane is one of its most desirable properties and is especially valuable in thoracic surgery. Since the patient will resume control of his own breathing when desired, there is no fear of respiratory depression from the use of relaxants.

An interesting sidelight in the investigation was the occurrence of low minute and tidal volume readings in the premedicated cases, many of which were surprisingly depressed.

Although only one patient with asthma was anaesthetized with Fluothane, the relaxation of bronchospasm produced suggests another possible advantage of this agent

The decrease in bronchial secretions suggests a future for Fluothane in thoracic surgery, though there was an impression that with an open chest blood pressure was difficult to maintain

Recovery from anaesthesia was assessed and there seemed to be an increase in the time taken to recover consciousness with increasing duration of surgery. The majority of patients were responding well within 45 minutes after anaesthesia was discontinued, and most were fully conscious after about 60 minutes. With procedures lasting 4 hours and more, consciousness was regained after approximately 90 minutes.

Relaxation generally could be described as moderate. Lower abdominal incisions could usually be closed without the need for a relaxant, but unless Fluothane had been administered for three hours or more, upper abdominal wounds required the use of one.

After three hours, with controlled respiration relaxation became excellent, and many surgeons commented favourably.

An interesting observation has been the brief duration of action of the curare-type relaxants. The explanation for this is unknown.

Postoperative vomiting is probably much less than with other agents. In the closed circuit series, 3.3 per cent of the patients vomited within the first four hours postoperatively, and 8.5 per cent within the first 24-hour period. The corresponding figures in the semi-closed series were 8 per cent and 13.7 per cent respectively. It should be recalled that more than half were neurosurgical cases.

Generally speaking, the authors feel that Fluothane has sufficient desirable properties to justify its inclusion in the anaesthetist's armamentarium, though further work on the possible metabolic effects is needed.

Because it causes a profound depression of the cardiovascular system, Fluothane probably should be used only by the experienced anaesthetist We do not feel it is suitable with present-day equipment for the occasional anaesthetist. Although some means of knowing the exact concentration in the circuit would be interesting and safer, differences in individual sensitivity to Fluothane could still occur. Therefore, the blood pressure reading is still the most important guide to the patient's safety.

We feel that Fluothane will be used mostly in neurosurgery, plastic and radical surgery, and certain cases involving an explosion hazard.

SUMMARY

A series of 310 cases is presented in which Fluothane® has been administered, using both the closed and semi-closed techniques.

The chief advantages of Fluothane® are.

1. Non-explosibility.
2. Can be used in the presence of soda lime.
3. Non-irritating to breathe.
4. Diminished salivary and bronchial secretions.
5. Diminished bleeding without the need for extreme hypotension.
6. Can be used as a reversible hypotensive agent
7. Allows respiration to be readily controlled.
8. Moderately rapid recovery.
9. Low incidence of postoperative vomiting.
10. Low incidence of postoperative hypotension and shock.

The chief disadvantages are.

1. Cardiovascular depression, often of severe degree.
2. Respiratory depression with moderately light anaesthesia. Apnoea with deeper planes.
3. Frequently causes cardiac arrhythmias.
4. Relaxation generally only moderate.
5 Incompatible with epinephrine and norepinephrine.

REFERENCES

1 ROBBINS, B H Preliminary Studies of the Anaesthetic Activity of Fluorinated Hydrocarbons J Pharmacol & Exper Therap , *86* 197 (1946)

2. RAVENTÓS, J The Action of Fluothane A New Volatile Anaesthetic Brit J Pharm & Chem , *11* #4, 394 (1956)

3 JOHNSTONE, M The Human Cardiovascular Response to Fluothane Anaesthesia Brit J Anaesth , *28* 392 (1956)

4 ORTH, O S & DORNETTE, W H L Fluomar as an Anaesthetic Agent Fed Proc , *14* 376 (1955)

5 GAINZA, E , HEATON, C E , WILLCOX, M & VIRTUE, R W. Physiological Measurements during Anaesthesia with Fluomar Brit J Anaesth , *28* 411 (1956)