THE HUMAN CARDIOVASCULAR RESPONSE TO FLUOTHANE* ANAESTHESIA

BY
MICHAEL JOHNSTONE

Department of Anaesthetics, Royal Infirmary, Manchester

with the 1 per cent vapour concentration used for maintenance.

Histopathological studies revealed minor cytological changes in the livers and kidneys of experimental animals after prolonged Fluothane anaesthesia. These changes did not appear to be associated with significant functional or biochemical alterations.

In view of the rather attractive pharmacological properties of this drug a clinical trial was begun. This paper is a report on the effect of Fluothane on some 500 patients. The list of operations performed on them is given later. Some of the patients would come under the heading of “good risks”, whilst others could be described as “grave risks” and a still greater number would fall into intermediate categories. This initial report will be concerned mainly with the cardiovascular effects of Fluothane when administered from a Boyle’s apparatus.

**METHOD**

The smaller (Trilene) bottle of a Boyle’s apparatus was found to provide a vapour and gives the approximate vapour concentration of from 0.2 to 4.2 per cent tration as calculated from a chart provided at 25°C. with a gas flow of 10 litres a for this particular vaporizer. In all cases minute, Fluothane filled to the 100 ml the 10-litre gas flow remained constant and consisted of 5 litres of oxygen and 5 Under similar circumstances with 50 ml litres of nitrous oxide; the plunger was of Fluothane in the bottle the plunger always fully withdrawn; and the liquid range was 0.1 to 2.8 per cent. With the maintained approximately at the 50 ml plunger fixed at 3 mm above the surface mark.

Blood pressures were estimated by sphygmomanometry and radial pulse palpation in all cases before induction and at frequent intervals thereafter. Respiratory obtained when using this equipment for rates were recorded at frequent intervals. Continuous electrocardiography was used

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Premedication

Atropine only, 0.6 mg thirty minutes before induction ................ 108 cases
Atropine 0.6 mg with pethidine 50 mg before induction ............... 392 cases

Induction of Anaesthesia

In all cases, except where otherwise stated, anaesthesia was induced with a sleep dose of thiopentone (250 mg) injected intravenously followed by 50 mg of suxamethionium and oropharyngeal or orotracheal intubation. The induction of anaesthesia with Fluothane will be made the subject of a separate study and report.

Series One. Vapour concentration 2.2 to 3.2 per cent approximately; lever mark 7 to 8; plunger fully withdrawn; 50 ml of Fluothane in the bottle.

This initial series consisted of fifty adults with normal cardiovascular and respiratory systems undergoing operations such as hemiorrhaphy, mastectomy, thyroidecomy (nontoxic), varicose vein, and various orthopaedic procedures. Each operation lasted a minimum of twenty-five minutes and took place with the patient in the supine position. Each patient was premedicated with atropine 0.6 mg and pethidine 50 mg and an airway inserted under the thiopentone suxamethionium sequence. Respiration was then controlled with oxygen, nitrous oxide and Fluothane (mark 7 or 8) until the return of spontaneous respiration a few minutes later. Anaesthesia was then maintained with a similar mixture till the end of the operation.

Smooth anaesthesia persisted throughout the period of operation in all cases, without narcotic or relaxant supplementation. Adequate relaxation was always present. The respiratory rate tended to increase during Fluothane anaesthesia and particularly with surgical stimulation, the average rate during the operations being 28 respirations a minute. The transition from suxamethionium apnoea to spontaneous respiration under Fluothane anaesthesia was made without coughing or straining. In each case reflex activity returned within two or three minutes of stopping the anaesthetic and was followed by a five- to ten-minute period of apparently natural sleep from which the patient invariably became slower and rates as low resented being roused. Full consciousness as 45 beats a minute were observed. Atropine then returned and was not associated with ventricular nodal rhythms were seen in any restlessness, retching, or vomiting; five patients, atrioventricular dissociation none of the patients complained of nausea with interference in two, and an unusual

As the blood pressure fell during a five- to ten-minute period of apparent Flueothane anaesthesia the pulse rate fell in 35 cases the systolic pressure dropped to between 60 and 80 mm Hg and the hypotension was associated with brisk vasodilatation with an increase in the volume of the peripheral pulse; the skin became warm, dry, and pink, and remained in this state throughout the period of anaesthesia. There was after initial falls to 80 mm Hg, rose gradually to 100 mm Hg and persisted at this level for the remainder of the operations.

Male, 48 years. Fit and muscular. Nephrectomy for stone. Premedicated with atropine 0.6 mg with pethidine 50 mg. All Lead 2.
A. Before induction.
B. After thirty minutes Flueothane (scale mark 8) anaesthesia; note the unusual coupling of the sinus beats.
C. Thirty seconds later, after atropine 0.5 mg intravenously.
In nine patients the hypotension outlived the narcosis by twenty minutes. There were no increases in pulse rates during the recovery periods, and in several patients the rates tended to decrease as the blood pressure returned to normal.

**Series Two.** Vapour concentration 0.75 to 1.25 per cent approximately; lever mark 6 to 7; plunger fully withdrawn; 50 ml of Fluothane in the bottle.

Fifty patients, with normal cardiovascular and respiratory systems, undergoing operations similar to those in the previous series. Each patient was premedicated with atropine 0.6 mg and pethidine 50 mg administered intramuscularly thirty minutes before induction. An additional dose of 0.5 mg of atropine was mixed with the deep dose of thiopentone, suxamethonium 50 mg injected and an airway inserted. Anaesthesia was then maintained with oxygen, nitrous oxide 50 per cent, and Fluothane (1 per cent approximately). This concentration provided smooth and even anaesthesia with adequate spontaneous respiration and sufficient relaxation for all the operations. The respiratory rates increased to an average of 30 a minute; this rate could be reduced to any required level by the intravenous administration of pethidine in doses up to 40 mg. The recovery phases were similar in all respects to those in the previous series, except that one patient vomited a few times and two complained of nausea. The patient who vomited stated that she became nauseated shortly after the pethidine was administered pre-operatively and she vomited twice before the induction of anaesthesia. During cold weather it was noted that several patients shivered for a few minutes after recovering consciousness; the shivering required no specific treatment.

The incidence of hypotension was considerably less in this series. The systolic pressures fell to 70 mm Hg in six patients and in the remainder the average systolic pressure during the maintenance of anaesthesia was 100 mm Hg. The mild hypotension associated with Fluothane (1 per cent approx.) anaesthesia persisted throughout the period of anaesthesia in most cases, but in sixteen patients the systolic pressures gradually returned to within normal limits after thirty minutes anaesthesia. A perfectly regular sinus rhythm persisted throughout anaesthesia in all cases, the average rate being 84 beats per minute. Heart rates in general tended to decrease slightly as the operation progressed, and there were no reactionary tachycardias in any patients during recovery from anaesthesia. Throughout the period of anaesthesia in each case the skin remained warm, dry, and pink, with prominent superficial veins. The cardiograms showed no significant changes in the ST segments or T waves.

**PRELIMINARY CONCLUSIONS**

The results obtained in this series indicated that Fluothane provided very smooth and easily reversible anaesthesia with adequate relaxation for the operations selected. Although relaxation was of a high degree there was no obvious evidence of respiratory depression with the vapour concentrations used. The effects on the cardiovascular system—hypotension and bradycardia—were consistent with a depression of sympathetic activity with sparing of the cardiac parasympathetic mechanism—a syndrome very similar to that induced by high spinal when tachycardia was present or when analgesia. Other signs suggestive of depression of autonomic activity were the sary to limit bleeding, e.g. neurosurgery, persistent vasodilatation, the complete mastectomy, etc. Fluothane was used in absence of sweating, the complete suppression of salivary, bronchial, and gastric secretions, and the absence of vomiting and retching in the recovery period.

It is obvious that the intensity of the cardiovascular reaction to Fluothane anaesthesia is directly related to the concentration of Fluothane used, being minimal with the 1 per cent which appears to be the concentration needed for maintenance in most cases. Many of the patients felt quite hungry and were able to enjoy substantial meals within two or three hours of the operations. There were no obvious signs of postoperative damage to kidneys, liver, or lungs, though the effects of Fluothane on the functions of these organs will be the subject of more detailed investigations.

In view of the encouraging results obtained in the preliminary studies, the use of Fluothane was immediately extended to cover most types of surgical operations on patients with either normal or abnormal cardiovascular and respiratory systems. The only patients excluded were those with obviously diminished or elevated blood pressures pre-operatively. An additional 400 cases have now been completed, their ages ranging from 7 months to 86 years. Premedication was either atropine 0.6 mg alone or combined with pethidine 0.5 mg; anaesthesia was induced with a sleep dose of thiopentone (unless otherwise stated) and an airway inserted after suxamethonium paralysis. The additional 0.5 mg of atropine was usually injected
Fluothane provided excellent relaxation patients were often sensitive to changes for all these cases with the exception of posture, and the reversed Trendelenberg laparotomies, some of which required bung position sometimes precipitated a supplementation with relaxants. Adequate profound hypotension. Sudden loss of spontaneous respiration was present before during anaesthesia was associated throughout the operations and seldom with a sudden fall in the systolic pressure required any assistance. In the majority of without much change in the pulse rate; patients the administration of Fluothane the reaction to the transfusion of blood or caused an increase in the respiratory rate, saline was rapid. Traction on abdominal the depth remaining either unaltered or viscera or retraction of brain tissue caused slightly increased. Surgical stimulation, sudden drops of blood pressure with slow—particularly in the region of the anus, ing of the pulse rate in about 20 per cent often caused an increase in the respiratory of the patients subjected to these rate, and rates up to 60 a minute have manœuvres. been encountered during haemorrhoidectomy. These rapid rates were not associated with any increase in the resistance of the lungs to inflation nor was there any vascular reactions to Fluothane. The hypotension associated with Fluothane anaesthesia can be prevented or immediately abolished by the intravenous injection of methoxamine hydrochloride, which can be controlled with pethidine in doses up (Cummings and Hays, 1956) in 5-mg doses. This drug has invariably produced the desired effect and is much more consistent in its vasopressor action than other methonium.

Brisk reflex activity returned in two or drugs of this type. It has not caused any three minutes after stopping the Fluothane cardiac arrhythmias or tachycardias when thane in all cases and vomiting during administered to patients anaesthetized recovery was present in about 4 per cent with Fluothane. The dose should be careof patients, being most evident after fully restricted, as excessive amounts—cholecystectomy. Transient postoperative 10 mg and over—may cause severe nausea was present in 8 per cent of the hypertension. Methoxamine completely prevents the hypotension associated with the head-up position.

Fluothane in the concentration range of 0.75 to 1.25 per cent caused a moderate drop in blood pressure in most cases and a drop to 90 mm Hg in 10 per cent of cases. After twenty or thirty minutes Cardiac Rhythm during Fluothane Anaesthesia.

Sinus rhythm has persisted at a steady rate throughout anaesthesia in most cases. Returned to within normal limits in about half of these patients. Anaesthetized treemly rare, probably as the result of the hormone and is suspected to be related to the hypokalaemia.

Relaxants and Fluothane.

The use of relaxants to facilitate the exploration of the peritoneal cavity is probably advisable when using Fluothane nowadays expected by the surgeons may result in unnecessarily severe degrees of hypotension requiring postural adjust-ments.

In the initial stage of this part of the investigation 15 mg of d-tubocurarine were injected intravenously into each of ten patients anaesthetized with Fluothane for 270 minutes (scale mark 7); laparotomy for appendicitis was being performed on each and the d-tubocurarine was injected as the peritoneum was being incised. Following the injection of d-tubocurarine in each case there was an immediate drop in blood pressure to between 60 and 70 mm Hg, without significant change in the pulse rate.

Controlled respiration was then necessary in three patients, and in one of these the peripheral pulse disappeared completely during positive pressure inflation of the lungs, and a cyanotic pallor developed; the slightest pressure on the rebreathing bag obliterated the carotid pulse which returned slowly and sluggishly when the pressure was withdrawn. The appendicectomy was hurriedly completed and neostigmine 2.5 mg with atropine 0.5 mg were administered intravenously. As soon as spontaneous respiration commenced there was a dramatic im-
Fluothane anaesthesia. It caused no further fall in systolic pressure, in fact, by from 10 to 15 mm Hg. Similarly, consciousness did not produce any obvious impairment returned in fifteen minutes and the systolic of the peripheral circulation. Over 200 pressure became normal two hours later; patients have now received suxamethonium subsequent recovery was uneventful. tonium 50 mg intravenously under Fluothame. similar syndromes of somewhat less than anaesthesia without any adverse alarming degrees occurred during anaesthesia systems. In trolled respiration in the other patients, the management of abdominal cases a All patients seemed to be hypersensitive to small dose of suxamethonium (30 to 50 the inhibitory effects of neostigmine on mg) is given intravenously as the peri- heart and required unusually large dosages of atropine to counteract this effect.

For the subsequent twenty adult laparotomies the dose of d-tubocurarine was peritoneum when the suxamethonium is restricted to 5–10 mg, depending on the repeated, the Fluothane providing adequate size of the patient. This dosage produced quae relaxations and spontaneous respiratoinsatisfactory relaxation with spontaneous respiration which required assisting in a few cases. Two mitral valvotomies were successfully performed with this technique, using only assisted respiration electrocardiographic evidence of myocardial insufficiency—eight of them had angina of mark 62)—was quite adequate, the doses of atropine being 50 mg per cent, and Fluothane (scale mark 7).

Heart Disease and Fluothane Anaesthesia. Seventeen patients with clinical and Heart Disease and Fluothane Anaesthesia. Seventeen patients with clinical and echocardiography evidence of hypertensive heart disease have been anaesthetized with Fluothane for periods up to 2 hours without the development of any significant evidence of further myocardial damage. In these patients the systolic pressure did not fall below 100 mm Hg. The following case history illustrates one

**Case 1.** Male, 48 years. Muscular and well nourished. For transmural cardiac necroectomy for the relief of intractable angina of effort. The electrocardiogram showed inverted T waves in the six V leads, with erect T waves in the classical limb leads. No cyanosis, oedema, or arteriosclerosis. Lungs normal. Blood pressure 120/85. Premedicated with atropine 0.6 mg and pethidine 50 mg. A few minutes after arrival at the theatre the patient complained of severe precordial pain and dyspnoea. His pulse rate was 115 beats a minute and his blood pressure 120/80, and the electrocardiogram showed depression of the ST segment on lead 2 (fig. 3A). Anaesthesia was immediately induced with thiopentone 200 mg intravenously (without additional atropine) followed by suxamethonium 50 mg and orotracheal intubation; this caused no change in the electrocardiogram. Anaesthesia was then maintained with oxygen, nitrous oxide 50 per cent, and Fluothane (scale mark 7). Smooth spontaneous respiration returned in three minutes by which time the pulse rate had dropped to 88 beats a minute and was of much better volume, the systolic pressure had fallen to 70 mm Hg; the skin became warm, dry, and pink, and the ST segment returned to its normal isoelectric position (fig. 3B). Fifteen minutes later, just prior to the opening of the pleural cavity, 7.5 mg of d-tubocurarine were administered intravenously and respiration gently assisted to prevent the complete collapse of the left lung. For the next twenty minutes anaesthesia was maintained with Fluothane (scale mark 62), the systolic pressure persisted at 70 mm Hg, the pulse rate gradually slowing to a steady 65 beats a minute, and the skin remaining warm and dry. Fluothane was then discontinued and within five minutes, although the pulse rate and blood pressure were gradually rising, the skin became clammy and cool. Fluothane (scale mark 62) was started again and in and a few minutes the skin became warm and dry, the blood pressure stabilized at 70 mm Hg systolic and the pulse rate at 65 beats a minute. The operation was successfully completed after 80 minutes anaesthesia. Methoxamine hydrochloride 5.0 mg was injected intravenously at the end of the operation. Fifteen minutes later the patient was awake and rational with a blood pressure of 130 mm Hg systolic and a pulse rate of 88 beats a minute. Recovery was uneventful.

Eleven patients with electrocardiographic evidence of hypertensive heart disease have been anaesthetized with Fluothane for periods up to 2 hours without the development of any significant evidence of further myocardial damage. In these patients the systolic pressure did not fall below 100 mm Hg. The following case history illustrates one...
of the more severe hypertensives during Fluothane anaesthesia:

CASE 2. Female, 66 years. Cranio-tomy and removal of a right frontal glioma. Frail and thin. Fully conscious. Blood pressure 210/120 with electrocardiographic evidence of hypertensive heart disease (fig. 4A). No cyanosis or oedema, lungs normal. Premedication atropine 0.6 mg with pethidine 50 mg. Induced with thiopentone (without additional atropine) followed by suxamethonium 50 mg and orotracheal intubation. A severe derangement of cardiac function followed the injection of thiopentone (fig. 4B) and was abolished immediately (fig. 4C) by the rapid insufflation of Fluothane vapour (2 per cent approx. in oxygen); the patient was adequately oxygenated at the time of the appearance of this arrhythmia. Anaesthesia was then maintained for 342 hours with oxygen, nitrous oxide 50 per cent, and Fluothane (scale mark 6). During the period of anaesthesia the systolic blood pressure did not drop below 130 mm Hg and bleeding from the operation area was negligible. Blood replacement therapy was not necessary and the patient responded to instructions within fifteen minutes of the conclusion of the operation. Recovery was uneventful.

Effects of Fluothane on Cardiac Arrhythmias present before Induction. In six of these the ectopic beats disappeared completely during Fluothane anaesthesia. Atrial fibrillation was present in anaesthesia but returned with the return of consciousness; one of these cases is illustrated in figure 5. The incidence of fibrillation in two patients, mitral stenosis in ectopic beats in the seventh case was unchanged and the ventricular response decreased in each case. All patients made uneventful recoveries.

Frequent ventricular extrasystoles were observed in seven patients before operation. In six of these the ectopic beats disappeared completely during Fluothane anaesthesia but returned with the return of consciousness; one of these cases is illustrated in figure 5. The incidence of fibrillation in two patients, mitral stenosis in ectopic beats in the seventh case was unchanged and the ventricular response decreased in each case. All patients made uneventful recoveries.
been anaesthetized with Fluothane. In one case the pulmonary disease was secondary to severe kyphoscoliosis, the remainder being due to chronic bronchitis. Three of these patients had severe cor pulmonale syndromes with orthopnoea, cyanosis, and congestive heart failure at intervals. The operations were mainly prostatectomies. Each patient was premedicated with atropine and pethidine and anaesthesia was induced with the usual slow dose of thiopentone followed by suxamethonium 50 mg and the insertion of an airway; one patient was induced with Fluothane (scale mark 8) in oxygen. In each case the Fluothane anaesthesia was associated with smooth and easy respiration with the disappearance of the bronchiolar constriction associated with the disease; cyanosis disappeared and the patients became pink and well oxygenated; muscular relaxation was excellent and bleeding was minimal. Recovery of consciousness was prompt in all cases and there was no evidence of the shock syndrome. In the more severe cases there appeared to be an improvement in their respiratory functions postoperatively. Clinical details of one of these cases are as follows:

**CASE 3.** Male, 43 years. Haematuria and pyuria due to prostatic calculi. Severe kyphoscoliosis with cor pulmonale. Cyanosed, orthopnoeic, and confined to bed for the past six months; occasional oedema of the dependent parts. Blood pressure 135/90. Sinus rhythm, 125 beats a minute, with severe right ventricular failure. First anaesthetic.

Cystoscopy. Induced with thiopentone 250 mg intravenously followed by suxamethonium 50 mg and the insertion of an airway. Apnoea persisted for the next thirty minutes during which time the patient was ventilated with nitrous oxide in oxygen 30 per cent; during this period the pulse was rapid and feable, the systolic blood pressure 70 mm Hg and sometime much lower. A cyanotic pallor persisted throughout the period of anaesthesia and was associated with clammy sweating. Weak spontaneous respiration returned after thirty minutes and consciousness returned twenty-five minutes later. The patient was very distressed and dyspnoeic for several hours afterwards.

Second anaesthetic. Three months later, Fluothane now available. For suprapubic prostatectomy. Patient’s cardiac pulmonary condition unchanged. Patient arrived at the theatre in a severely orthopnoeic state, cyanosed and sweating, pulse rate 125 a minute, blood pressure 135/90; electrocardiograph showed sinus tachycardia with right ventricular strain (fig. 6A). Anaesthesia was induced with Fluothane (scale mark 8). After two minutes the patient was obviously unconscious but not adequately relaxed for easy intubation; 50 mg of suxamethonium were immediately injected intravenously and an orotracheal tube inserted without difficulty and without electrocardiographic disturbance. During the period of suxamethonium apnoea the patient’s lungs were very difficult to inflate but this difficulty disappeared with the return of spontaneous respiration three minutes later. For the next 90 minutes anaesthesia was maintained smoothly with Fluothane (scale mark 7). During this time respiration was spontaneous and offered no resistance to inflation. The systolic blood pressure was maintained at 70 mm Hg with a regular sinus rhythm at 110 beats a minute (fig. 6A). Respiration was excellent and bleeding was minimal—the operation was performed with the patient in the Trendelenburg position 30 degrees. Throughout the operation the patient’s skin remained warm, dry, and pink. Consciousness returned within fifteen minutes of stopping the anaesthetic and recovery was uneventful. After the operation the patient stated that his breathing felt easier than it had done for several months.

In addition to the emphysematous patients there were three patients with supplicative bronchiectasis and three with active pulmonary tuberculosis. There were no operative or postoperative pulmonary complications in any of these patients. During anaesthesia with Fluothane there was a complete absence of salivary, mucous, and bronchial secretions in these patients.

Jaundice and Fluothane Anaesthesia.

Eight adult patients with jaundice have been anaesthesized with Fluothane for periods up to two hours. In seven patients the jaundice was due to carcinoma of the head of the pancreas and cholecystoduodenostomy was done in each case; two of these patients had hypertensive heart disease, one with auricular fibrillation and intraventricular block. The eighth patient became jaundiced after an attack of acute cholecystitis. Each patient was premedicated with atropine 0.6 mg with pethidine 50 mg and anaesthesia was induced with the usual dose of thiopentone—followed by suxamethonium 50 mg and orotracheal intubation. Anaesthesia was then maintained with Fluothane (scale mark 7). Maintenance of anaesthesia was smooth and uneventful in all cases, without any clinical or electrocardiographic evidence of further cardiovascular damage; recovery of consciousness was as quick as in the nonjaundiced cases. Seven patients made uneventful recoveries, the jaundice gradually disappearing in two or three weeks; one patient, with carcinomatous deposits in the liver, died on the seventh postoperative day from the effects of biliary peritonitis.

Uraemia and Fluothane Anaesthesia.

Fluothane (scale mark 6 to 7) was administered to ten patients with uraemia secondary to urinary obstruction due either to prostatic hypertrophy or to ureteric obstruction by pelvic neoplasm. In addition, twelve elderly males were admitted with uraemia secondary to prostatism; normal blood urea levels were restored in each of these cases by preoperative catheter drainage. Details of the patients who were still uraemic at the time of operation are as follows:

**CASE 4.** Female, 48 years. Anuria of at least 48 hours duration, secondary to obstruction of both ureters by pelvic neoplasm. Blood urea 380 mg per cent; serum potassium 6·54 mEq/; blood pressure 170/100 mm Hg. Patient drowsy and dehydrated, radial arteries difficult to palpate, suggesting vasospasm of considerable degree; no visible or palpable veins on arms or legs. Premedicated with atropine 0·6 mg and pethidine 50 mg.

Anaesthesia was induced with Fluothane (scale mark 8) and an orotracheal tube inserted without difficulty and without electrocardiographic changes after two minutes (fig. 7A). Anaesthesia then maintained for the next 45 minutes with Fluothane (scale mark 7), during which time a left nephrectomy was performed without difficulty, relaxation being excellent, bleeding minimal, and spontaneous respiration remaining efficient.

Immediately after the induction of anaesthesia the systolic blood pressure dropped to 70 mm Hg and brisk vasodilatation occurred with the appearance of several large veins on the forearm was permitted the easy intravenous administration of fluids and glucose to combat the potassium intoxication. The.
electrocardiogram, which pre-operatively showed evidence of potassium intoxication (fig. 6), remained completely unchanged throughout the operation.

Consciousness returned five minutes after the cessation of Fluothane inhalations and the blood pressure returned to 170 mm Hg systolic a few minutes later. There was no postoperative nausea or vomiting. Immediately after the operation there was a steady flow of urine from the nephrostomy and three days after the blood potassium was subnormal (fig. 7), this was rectified by the oral administration of potassium. The blood urea, after a gradual rise to 440 mg per cent on the third day after the operation, had returned to normal by the 21st postoperative day.

Case 5. Female, 51 years. Anaemia for two days as the result of uterine obstruction by pelvic neoplasm. Fully conscious, condition good, blood urea 120 mg per cent, serum potassium normal. Induced and maintained with Fluothane for thirty minutes during which time urinary flow was re-established by the insertion of a ureteric catheter. Blood chemistry gradually returned to normal in seven days.

Case 6. Female, 53 years. Clinical details essentially similar to Case 5. After twenty minutes of Fluothane anaesthesia, a pre-operative blood urea of 153 mg per cent had returned to normal a week later.

Case 7. Male, 75 years. Acute retention of urine due to prostatic hypertrophy. Completely disoriented and anaemic, blood urea 135 mg per cent. Heart and lungs normal. Anaesthesia induced with thiopentone 250 mg (with additional atropine) and maintained by Fluothane (scale mark 7) for 65 minutes whilst a suprapubic prostatectomy was successfully performed. Consciousness returned fifteen minutes after the end of the operation and there was no evidence of shock. Twenty-four hours later the patient was quite rational and the blood urea returned to normal seven days after the operation.

Case 8. Male, 83 years, with prostatic hypertrophy. Blood urea 243 mg per cent on admission and reduced to 87 mg per cent after four weeks catheter drainage. A suprapubic prostatectomy was successfully performed under Fluothane anaesthesia lasting 55 minutes. Postoperatively there was a progressive rise of the blood urea level to 350 mg per cent on the 5th day; this was associated with a diuresis and normal blood electrolytes most of the time. Seven days later the blood urea had returned to 83 mg per cent and the patient had become ambulant and active.

Case 9. Male, 68 years, with prostatic hypertrophy. Blood urea on admission was 123 mg per cent and reduced to 74 mg per cent by seven days catheter drainage. Suprapubic prostatectomy then performed under Fluothane anaesthesia. Postoperatively the blood urea rose to 112 mg per cent on the third day and was within normal limits by the tenth day.


Case 12. Male, 63 years. Clinical details essentially similar to Case 9.


Deaths following Surgery under Fluothane Anaesthesia.

No deaths have occurred under Fluothane anaesthesia. Six patients have died in the postoperative period and the details are as follows:

(1) Female, 47 years. Bilateral adrenalectomy for generalized carcinomatus due to malignant disease of the breast. Pathological fractures of the ribs, pleural effusions, and multiple secondaries in the liver. Emaciated and anaemic. The bilateral approach to the adrenals was used and the patient tolerated the operation very well. Blood pressure remained within normal limits throughout and consciousness returned to normal limits on the 3rd day. The patient died 48 hours later from a massive haemorrhage.

(2) Male, 61 years. Died seven days after a supra-pubic prostatectomy. Autopsy revealed bilateral suppurative pyelonephritis and of suppurative bronchectasis. Cause of death was toxania due to sepsis.

(3) Male, 68 years. Aneurysm secondary to cerebral atrophy as the result of cerebral arteriosclerosis. Bedridden and incapable for several months. Scattered motor sounds at both lung bases. Cerebral angiography and pneumoencephalography performed under Fluothane anaesthesia of 65 minutes duration. Consciousness and full reflexes returned within fifteen minutes without any evidence of shock or collapse. Prior to recovery of consciousness considerable amount of purulent sputum was aspirated from the bronchi. The patient died 48 hours later from what appeared to be hypostatic pneumonia. Autopsy revealed a terminal bronchopneumonia.

(4) Baby, seven months old. For removal of a huge meningoencephalocele. Heart and lungs normal. Premedicated with atropine 0.4 mg. Anaesthesia induced with Fluothane (scale mark 8). Intubation of the trachea was impossible because of the extreme degree of neck flexion caused by the tumour. A nasopharyngeal tube was inserted and anaesthesia smoothly maintained for the next 21/2 hours with Fluothane (scale mark 7). During this time the meningocele was excised along with a large amount of brain tissue. Blood loss was moderately severe and was not satisfactorily replaced. The baby commenced to cry and move its limbs within five minutes of stopping the anaesthetic. Death occurred twelve hours later and permission for autopsy was not obtained.

(5) Male, 73 years. Cystoscopy and suprapubic prostatectomy. Pit and well nourished. Heart and lungs normal. Blood pressure 170/100. Blood urea 105 mg per cent. Twenty-six years history of diabetes mellitus having insulin 20 units twice daily with appropriate diet. Blood sugar immediately before operation was 240 mg per cent. No urinary evidence of ketosis. Premedicated with atropine 0.6 mg and pethidine 50 mg. Anaesthesia induced with thiopentone 250 mg (with additional 0.4 mg atropine and 0.1 mg mepromazine) and the insertion of an airway. The operation was performed under Fluothane (scale mark 1) without difficulty in 75 minutes. Recovery was adequate without relaxants, bleeding was minimal and the intraocular blood pressure did not drop below 110 mm Hg. Blood transfusion was not required. Recovery from anaesthesia was complete in fifteen minutes.

Twelve hours later the patient became restless and the blood sugar rose to 480 mg per cent. The appropriate therapy was instituted, but the response was unsatisfactory, and the patient died from what appeared to be peripheral circulatory failure 36 hours later. During the first 24 hours postoperatively there was a satisfactory urinary output. Hypokalaemia was not excluded. Autopsy failed to reveal the cause of death.

(6) Female, 41 years. Craniotomy and partial removal of a pituitary tumour. Obese, Heart and lungs normal. Premedicated with atropine and pethidine; Anaesthesia induced with Fluothane (scale mark 7). Anaesthesia induced with Fluothane. Consciousness returned within fifteen minutes after the end of the operation and the patient’s condition was excellent for the next twenty-four hours. A sudden and unexpected collapse then occurred and the patient died within a few minutes. Autopsy failed to reveal the cause of death.

DISCUSSION

The general picture of the human cardiovascular system during Fluothane anaesthesia is one of vasodilatation combined with hypotension and bradycardia. The vasodilatation—as evidenced by dry warm, and pink skin with prominent superficial veins—becomes obvious within a few seconds after the start of inhalations and persists throughout the period of anaesthesia, even when minimal concentrations of vapour are inhaled. It does not appear to be affected by haemorrhage or by surgical stimuli.

The hypotensive effect is directly related to the inhaled vapour concentration being minimal with the lower concentra-
The apparently complete protection which Fluothane anaesthesia has provided against surgical shock in this investigation may be related to a suppression of sympathetic activity during anaesthesia. Evidence is accumulating which indicates that blockade of the sympathetic division of the autonomic nervous system during surgery prevents the type of circulatory collapse which may lead to death (Martin, 1955; Overton and De Bakey, 1956; Ross and Herzeg, 1956; Hershey et al., 1956). The excellent results obtained with Fluothane anaesthesia in patients with severe pulmonary emphysema and cor pulmonale may also be related to its effects on sympathetic ganglia: Bromage (1956) has recently demonstrated that ganglionic blockade caused significant increases in the vital capacities of patients with pulmonary hypertension.

As the result of recent clinical observations it has been suggested that Fluothane anaesthesia may be followed by a diuresis which may cause hypokalaemia in those patients who present evidence of electrolytic depletion prior to or after anaesthesia with Fluothane.

One elective Caesarean section was successfully performed under Fluothane (scale mark 7½) anaesthesia. Relaxation was adequate, bleeding minimal, the child was fully conscious when delivered from the uterus, and the uterus retracted normally after the removal of the placenta. Recovery of consciousness was complete in seven minutes after the removal of the tourniquet, and an unusual form of sinus face mask and there was no evidence of shock, vomiting, retching, or nausea.

**SUMMARY**

1. Fluothane—a new nonexplosive volatile anaesthetic agent—has been administered to 500 patients, including many with cardiovascular, pulmonary, renal, and hepatic diseases complicating the surgical lesions. Each patient was premedicated with atropine, either alone or combined with pethidine, and anaesthesia was induced in most cases with a sleep dose of thiopentone.

2. Smooth and rapidly reversible anaesthesia has been maintained in all cases by the continuous administration of Fluothane vapour, using a Boyle’s vaporizer and a gas flow of ten litres a minute with 50 per cent oxygen and nitrous oxide.

3. Cardiovascular changes suggestive of depression of sympathetic activity have consistently been observed and which, to a certain extent, were modified by atropine and by the strength of the vapour concentration inhaled. The shock syndrome has been completely absent in all cases.

4. There has been a complete absence of salivary, mucous, and bronchial secretions in all cases throughout the period of anaesthesia. Nausea, vomiting, and retching during recovery have been absent in over 90 per cent of the patients.

5. Cardiac arrhythmias of the vagal type were observed when the higher concentrations of Fluothane vapour were inhaled. These arrhythmias included sinus bradycardia, atioventricular nodal recovery of consciousness was complete rhythms often with interference, dissociation in seven minutes after the removal of the tourniquet, and an unusual form of sinus
arrhythmia with coupling of the sinus beats. Atropine restored normal sinus to serious electrolytic depletion in those rhythms in these cases. Their incidence has been completely eliminated by adequate atropinization.

6) Ventricular arrhythmias have been observed only in the presence of inadequate ventilation in lightly anaesthetized subjects and were of a mild degree. Ventricular tachycardia has not been observed.

7) Cardiovascular collapse—slow pulse and profound hypotension—has followed the combined use of d-tubocurarine and controlled respiration on patients anaesthetized with Fluothane. Such reactions did not occur when suxamethonium and controlled respiration were used in conjunction with Fluothane anaesthesia.

8) Tachypnoea has occurred during surgical stimulation in patients lightly anaesthetized with Fluothane. The reaction can be controlled by pethidine or by regional nerve block.

9) No deaths have occurred under anaesthesia. The details of six postoperative deaths have been presented.

10) It has been suggested that Fluothane anaesthesia may cause an immedi-