A REVIEW OF FLUOTHANE *

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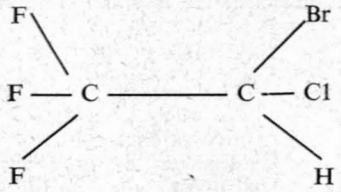
The advent of a new drug into the world of anaesthesia is an event of considerable interest, particularly when it is no mere variation on a proprietary theme. Fluothane, is certainly not this, nor indeed does it belong to the group of substituted ethers such as methyl-propyl (Neothyl), vinyl-ethyl (Vinomar), or trifluoro-ethyl-vinyl (Fluomar). It is original in being a halogenated ethane, a chemical group which, as such, has received little attention since John Snow advocated the use of dichlorethane in 1851.[1] In fact, it was while Snow was describing the clinical use of dichlorethane in the final chapter of his book 'On Chloroform and Other Anaesthetics' that he was seized with the illness

* A paper presented at the South African Medical Congress, Durban, September 1957.

which led to his untimely death in 1858 at the age of 40. However, one should perhaps remember that the simplest chlorinated ethane in everyday use is ethyl chloride.

Compared with other well-known anaesthetic agents, Fluothane is reasonably stable. But even an anaesthetist can recognize that the halogen acids might be potential breakdown products of a substance with this chemical structure:



It is known that fluorine is more electro-negative than the other halogens, and therefore one would expect these atoms to be firmly bound to their corresponding carbon atoms. At the same time this strong electro-negative potential tends to unbalance and weaken the linkage to the other carbon atom so that, on theoretical grounds, the most likely consequence of any decomposition would be the liberation of bromine and chlorine. Clinically there has been no evidence of the effects of any decomposition, although it is known to occur in the presence of light with moist air or oxygen. Even in the absence of light, moist air or oxygen allows a rapid reaction to occur between certain metal alloys and Fluothane vapour. This may take the form of a crust of tin bromide or chloride on the tin-foil lining of bottle caps, or actual pitting of aluminium surfaces. This property is of great importance in constructing a vaporizer from which accurately measured concentrations must be delivered; corrosion will take place unless suitable metals are employed throughout, or aluminium and tin surfaces (also any soldered seams) are 'protected' by anodizing, or by coating with nylon or other resistant plastics. Apart from the technical problems involved—and these can be overcome—there is no evidence at present to suggest that decomposition should be regarded any more seriously than it is in other well-known anaesthetic agents.

By far the most important property of Fluothane is its non-flammability in air and non-explosibility in oxygen in any mixture. On these grounds alone the drug merits a thorough assessment to see how far it answers the anaesthetist's criterion of a 'non-flammable ether' in terms of all-round efficiency and safety. The physical, chemical, and pharmacological properties of Fluothane have already been described in some detail.[2,3] Certain aspects undoubtedly need to be clarified, particularly the mechanisms by which the circulatory, respiratory, and sympathetic nervous systems are affected during anaesthesia. However, a discussion on these points would be profitless at this time; the sole object of this paper is to review the clinical aspects of its use.

The evidence is based on rather more than a thousand administrations in which Fluothane has been the sole or principal anaesthetic agent. Although there was no other selection of patients by age, physical fitness, or type of operation, it was not used in the more heroic procedures. Furthermore, it was tested on a number of volunteers to determine the effects of varying concentrations. Administrations were by the open drop technique, from a Boyle-type apparatus with nitrous oxide and oxygen, or from an E.M.O. inhaler[4] which had been specially calibrated and modified for use with Fluothane.

In unpremedicated subjects it was found that 0·5% Fluothane in air had little effect. Prolonged inhalation in this concentration caused no loss of consciousness and little, if any, analgesia, but 1% Fluothane in air regularly produced unconsciousness, and often a sufficient depth of anaesthesia for simple operations. In normal clinical use, slightly higher concentrations were needed to produce muscular relaxation, but it was never necessary to exceed 3%. However, even with this concentration, it was not always possible to provide ideal conditions for upper abdominal surgery. This may well have been the result of depressed respiration limiting the quantity of drug inhaled, a situation comparable to that found during cyclopropane anaesthesia, and one which can be overcome by assisting respiration.

TECHNIQUE OF ANAESTHESIA

Induction

Induction can be carried out with Fluothane alone,[5] or combined with nitrous oxide. In all instances consciousness is lost rapidly, without the accompanying sensation of suffocation so common with most inhalation anaesthetics. Coughing and breath-holding are rare, although occasional periods of apnoea within the first few minutes are not unknown. These do not appear to be associated with laryngeal spasm, for inflation of the lungs may be performed easily. In some cases, but by no means always, the condition is probably caused by a high concentration of Fluothane vapour. Since it may persist for several minutes, inflation is often necessary to avoid cyanosis, particularly if respiration has not already been restarted by applying a painful stimulus to the patient.

An excitement stage is unusual, and can be avoided, as also can the apnoea of induction, by a preliminary injection of thiopentone. For these reasons alone it is helpful to render the patient unconscious with a 'sleep dose' of thiopentone before proceeding with the administration. Repeated swallowing is not uncommon during the early stages of anaesthesia, but can be ignored since it does not presage coughing, breath-holding, or vomiting. At the same time, flushing of the skin, suffusion of the conjunctiva, and dilatation of the superficial vessels, are noticed. These seem to be more marked than under other forms of general anaesthesia and suggest an early effect on the sympathetic system. The observation has no practical significance, but the anaesthetist will appreciate another effect on the autonomic nervous system which causes depression of pharyngeal and laryngeal reflexes. Thus, with early relaxation of the masseter muscles, an oral airway may be inserted without provoking any response at a stage when the patient is still capable of moving. Further, even more vigorous stimulation such as touching the glottis with an endotracheal tube will not initiate spasm. At this stage the cords may come together, or there may be a cough, but normal respiration will be resumed within half a minute.

Maintenance of Anaesthesia

Anaesthesia may be maintained with Fluothane alone or combined with nitrous oxide and oxygen for all types of surgery except, as has been suggested already, where an

extreme degree of relaxation may be required for an upper abdominal operation. In any case, there is probably no justification for attempting to produce such deep anaesthesia by administering the higher concentrations of Fluothane for more than short periods of time. This is because of the effects on the respiratory and circulatory systems which, although apparent early on, undoubtedly vary with the concentration of vapour inhaled. To overcome this difficulty, thoughts immediately turn to the use of muscle relaxants. Of these, small doses only are needed to produce the desired results, but while suxamethonium may be administered as with any other anaesthetic sequence, d-tubocurarine and gallamine deserve special mention. In other instances, particularly in children, where for any reason prolonged anaesthesia with Fluothane is considered undesirable, ether would be the agent of choice. The change-over can be effected smoothly and quickly without risk of coughing or laryngeal spasm. Also, being a respiratory stimulant, the inhalation of ether will counteract any respiratory depression due to Fluothane.

Effect of Fluothane on the Respiratory System

Probably the most significant effect that Fluothane exerts on the body is that on the respiratory system.[6] Even in volunteers who had received no premedication and no preliminary injection of thiopentone, respiration could be reduced to a dangerously low level within a few minutes by the inhalation of 1% Fluothane vapour. On occasion a slow respiratory rate is seen, but more usual is a tachypnoea associated with a reduction in the minute volume. As the concentration of Fluothane vapour is increased, so the respiratory rate rises and the minute volume falls, giving a reduced tidal exchange (Fig. 1). This is made manifest by cyanosis when Fluothane and air are administered to the patient but, in the presence of oxygen, the colour will remain good even though the respiratory exchange is inadequate.

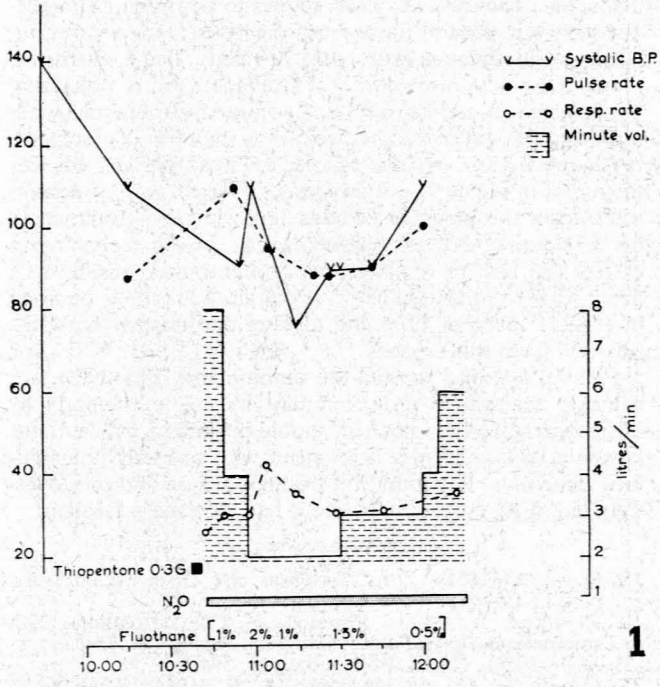


Fig. 1. Prostatectomy. Age 52. Premedication with 1/100gr. of atropine. The minute volume varies with the concentration of Fluothane vapour. As the minute volume falls, so the respiratory rate increases. The pulse rate and blood pressure tend to follow each other and are also influenced by changes in the concentration of Fluothane.

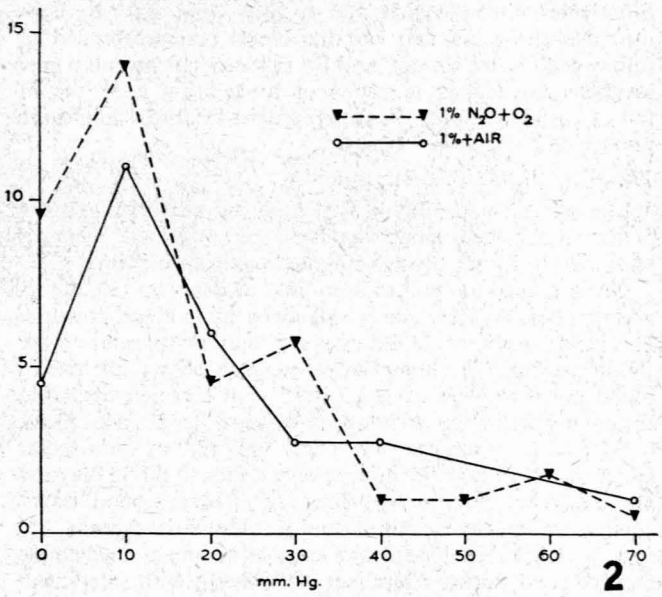


Fig. 2. Graph showing the maximum fall in blood pressure (systolic) after inhaling 1% Fluothane vapour for 5 minutes. Ordinates indicate the numbers of subjects in each group.

It is imperative that this effect should be fully understood by anyone contemplating the administration of Fluothane. A method of inflation must always be available and respiration must be assisted on the least suspicion. Failure to do so will inevitably lead to a tragedy.

The depression of minute volume is related to some extent to the pre-operative medication that the patient has received. No more than 50 mg. of pethidine combined with 1/100 gr. of atropine, or the atropine alone, should be used, since heavier sedation will depress respiration still further.

Effect of Fluothane on the Cardiovascular System

Johnstone[7] has made an extensive electrocardiographic study of the effects of Fluothane on the heart. He regards Fluothane as a 'safe' anaesthetic agent in this respect, but insists that atropine should be given as premedication to avoid extreme sinus bradycardia, which otherwise may be encountered. A degree of bradycardia almost always occurs, but arrhythmias are not to be expected.

Hypotension is common, but is rarely extreme unless a high concentration of Fluothane is administered. The blood pressure tends to fall within the first few minutes of an anaesthetic, but thereafter remains constant unless it is influenced by additional factors or by raising the concentration of Fluothane. As a rule the general condition of the patient remains surprisingly good, and with the general appearance and strong pulse which can be felt at any artery, it is difficult to believe that any appreciable degree of hypotension is present. No variation was noticed in the blood pressure fall with Fluothane and air as compared with

Fluothane, nitrous oxide and oxygen (Fig. 2). In both instances the pulse rate and the blood pressure tended to follow each other closely, and on this account atropine may be recommended as a means of moderating a too rapid fall of blood pressure. In more extreme instances Johnstone recommends the use of Vasoxyl.

Fluothane and Muscle Relaxants

The use of suxamethonium in conjunction with Fluothane anaesthesia is not remarkable and the results are identical with the use of this drug during any other anaesthetic.

Gallamine tri-iodide has been used in doses up to 120 mg. and on occasion there has been a slight fall in blood pressure. However, since the blood pressure and pulse rates under Fluothane tend to be parallel, there may be a slight rise in blood pressure probably associated with the tachycardia so commonly seen when gallamine is used in other circumstances.

With d-tubocurarine the effect on the cardiovascular system tends to be more dramatic, and falls in blood pressure are seen more commonly. They are often profound, particularly when the concentration of Fluothane exceeds 1% v/v. It would thus appear that suxamethonium and gallamine may be used during Fluothane anaesthesia with safety, but that d-tubocurarine should be employed only with caution, if at all. Neostigmine must also be considered in relation to the muscle relaxants, and its effects are of equal significance. Under Fluothane anaesthesia a much more profound fall in pulse rate is likely to be seen than usual, and this may be associated with a calamitous degree of hypotension. Such a response can be avoided by giving a large dose of atropine, at least 1/75–1/50 gr., 5 minutes before an injection of neostigmine. Neostigmine must then only be given in small divided doses at a rate not exceeding 1 mg. per minute, with 2·5 mg. as the maximum dose.

Recovery

Recovery from Fluothane anaesthesia is usually rapid but, naturally enough, will be influenced by any pre-operative drugs that may have been administered and any other supplementary medication. Apart from these, consciousness is usually regained within about 10 minutes of stopping the administration, provided that the patient has an adequate respiratory exchange. Recovery is characterized by a surprisingly rapid return of mental alertness and also, since Fluothane has little analgesic effect, the early appreciation of pain. In children this often leads to restlessness, which is best treated by the administration of an analgesic drug.

Nausea and vomiting are less than after most anaesthetics, and the patients commonly state that they feel fit. In a few instances, bouts of shivering may occur before full consciousness returns. These cannot be explained, but they may be provoked by painful stimulation.

DISCUSSION

Fluothane has many advantages, of which non-flammability, smooth and rapid induction, simple methods of administration, and quick recovery without undesirable side effects, are the most important. To these may be added freedom from irritation of the respiratory passages, the apparent absence of damage to the liver and kidneys, and often a bloodless operating field. But these claims must be balanced against depressed respiration, hypotension, bradycardia and the cost of the drug. The significance of the effects on the heart are not yet fully appreciated, nor are the mechanisms by which the changes in respiration and circulation are brought about. However, serious depression of respiration, even at light levels of anaesthesia, must be regarded as a warning against the injudicious use of the drug in unskilled hands.

It might have been hoped that Fluothane could replace chloroform in domiciliary practice; but where an open drop technique is chosen it is unlikely that efficient means of resuscitation will be immediately to hand. Also, since domiciliary practice implies obstetrics, one further difficulty remains. Although as an anaesthetic for the mother Fluothane has proved satisfactory, convenient and safe, yet it does pass the placental barrier and produces a fall in the foetal heart rate, often commensurate with the maternal bradycardia. Thus the obstetrician may be faced with the dilemma of deciding whether a slow foetal heart rate is due to foetal distress or to Fluothane.

CONCLUSION

Fluothane has proved to be an ideal agent for the induction of anaesthesia, and I regard it as being superior to ethyl chloride not only in children but also in adults. It can also be used in preference to trichlorethylene in a nitrous oxide and oxygen sequence because of the wider range of anaesthesia it produces and the ease with which the depth of anaesthesia may be altered. For major surgery requiring complete upper abdominal relaxation, I do not think that any real advantage can be claimed, although different techniques and methods of use might well alter this view.

With adequate precautions the open drop method of administration is satisfactory, although the criticism may be raised that the concentration of vapour administered is unknown. The same criticism applies to any open technique, but with our present limited experience of such a powerful agent as Fluothane it is probably justified. To be consistent, though, the administration of Fluothane from a vaporizing bottle which cannot be calibrated accurately and permanently must also be condemned,[8] especially as such pieces of apparatus as the E.M.O. and the Fluotec are available and efficient in use. Fluothane is not supposed to undergo any decomposition in the presence of soda lime; but the employment of a closed-circuit technique, even though economical, carries the risk of a dangerous concentration of the drug being reached in the system. An overdose may thus be given in a short space of time and already one tragedy has been reported from this cause.[9]

Finally, I would express the opinion that Fluothane is a valuable anaesthetic drug, but that its use, particularly by the inexperienced anaesthetist, should be limited and cautious. It would be a great pity if an agent with so many potentialities gained an evil reputation through misuse and misunderstanding of its properties before it had received a fair trial.

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