The addition of small doses of spironolactone permitted sodium diuresis with limited potassium loss, presumably by blocking electrolyte exchange in the distal tubules.

Corresponding doses of spironolactone, given alone, produced minimal sodium loss.

Large doses of spironolactone were ineffective in three patients with cardiac failure, but produced marked sodium loss in one patient with cardiac failure and in two patients with cirrhosis and ascites.

Aldosterone alone may account primarily for the sodium retention in patients with cirrhosis and established ascites, and may be the dominant factor also in some cases of congestive heart failure.

In most patients with congestive failure, changes of renal haemodynamics may be responsible for sodium retention. Our results suggest that these haemodynamic changes were not induced by an excess of circulating catechol amines.

Patients who responded to prednisolone showed a decrease of urinary aldosterone followed by a sodium diuresis.

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PORTABLE ANAESTHETIC APPARATUS FOR USE IN THE ANTARCTIC

BY

J. F. NUNN, Ph.D., M.B., Ch.B., F.F.A.R.C.S.

Leverhulme Research Fellow, Research Department of Anaesthetics, Royal College of Surgeons of England; Lecturer, Postgraduate Medical School, University of London; Honorary Consultant, Hammersmith Hospital, London

Expeditions are notoriously ill-equipped for the administration of a general anaesthetic. Current practice (to which the author has made no exception) is to rely upon local anaesthetics, thiopentone, and open ether. Since even experienced anaesthetists may find difficulty in the transition from thiopentone to open ether, it is perhaps fortunate that expeditions seldom offer an opportunity for the medical officer to exercise his skill.

This paper reviews the problem of anaesthesia in Antarctica and describes a technique which has been developed in conjunction with the Falkland Islands Dependencies Survey, the Medical Research Council (Division of Human Physiology), and British Oxygen Gases Ltd. The apparatus for this technique is now standard equipment with British and South African parties in Antarctica. It may also fulfil the requirements for general anaesthesia in other remote parts of the world.

It is not intended to discuss the merits of the alternatives to general anaesthesia. Clearly, local analgesia must be the method of choice when practicable, and, in Graham Land, Black (personal communication) has recently relieved and repaired a strangulated hernia under procaine field-block. Spinal analgesia is attractive to the single-handed medical officer, but carries dangers which cannot be overlooked. In addition, it is not applicable to the whole body and it is quite likely that an operation may outlast the effect of the drug.

Requirements of General Anaesthesia in Antarctica

It must be possible to provide anaesthesia for operations on any part of the body. Apart from trauma, the most likely operations are for appendicitis, strangulated hernia, and perforated peptic ulcer. Specialization in anaesthesia has hampered the training of undergraduates, and it can no longer be assumed that a newly qualified medical officer has acquired much skill or experience in anaesthesia. Thus it is essential to offer a simple technique. Furthermore, it is rare for an expedition to carry two medical officers, and it must therefore be possible for the maintenance of the anaesthetic to be delegated to a lay assistant. Inhalational anaesthetics should be non-inflammable, as open heating is used in the huts.

Size and weight of apparatus are now of less importance than formerly. A compact apparatus weighing a few kilograms is acceptable provided that large stocks of cylinders are not required. It may be assumed that an operation will be performed in a hut, caboose, or possibly a tent, where the temperature can be raised to at least 18° C., although during storage a fall to −70° C. is possible. Severe condensation follows the passage of warm fronts. Apparatus must also be

packed to withstand mechanical shock and exclude fine drift snow. Finally, all drugs and apparatus should have a shelf life of at least three years.

Halothane

The choice of a simple 100% potent anaesthetic has in the past lain between ether and chloroform, the former being safer and the latter easier to administer. The new agent halothane (" fluothane ") combines many of the advantages of both (Raventós, 1956 ; Brennan, Hunter, and Johnstone, 1957). There is a wide margin of safety, and, as with ether, anaesthesia may be carried to the point of respiratory arrest without cardiac failure. This is of prime importance if anaesthesia is to be maintained by a lay person. Halothane resembles chloroform in that its vapour is non-irritant and the narcotic blood concentration low. Induction is therefore easy. However, in one respect halothane falls short of the requirements of the ideal anaesthetic for an expedition. It is not unusual for the systolic blood-pressure to fall to levels of the order of 70–90 mm. Hg. Nevertheless, it is clear that this is due largely to a reduction in peripheral resistance rather than cardiac output (Payne, Gardiner, and Verner, 1959), and therefore tissue perfusion is generally unimpaired although at a lower pressure. There is as yet no evidence that this is harmful to a fit patient.

The maintenance of anaesthesia by a lay person is greatly simplified if he knows the inhaled concentration of the agent. Not only will this exclude the possibility of gross underdosage or overdosage, but the concentration may be readily altered in accord with the instructions of the medical officer. For these reasons it would appear advantageous to use a calibrated vaporizer compensated for temperature and flow rate of carrier gas.

The Case for Oxygen

Air is an ideal inspired gas for a fit person at a normal barometric pressure. The arterial oxygen tension is of the order of 100 mm. Hg, which is beyond the upper bend of the oxyhaemoglobin dissociation curve. Thus moderate underventilation may occur without significant desaturation of the arterial blood.

However, special considerations apply to general anaesthesia, particularly in Antarctica. Firstly, general anaesthesia often reduces the alveolar ventilation to two-thirds of the normal value (Nunn and Hill, 1960). Secondly, on the polar plateau the barometric pressure is of the order of 550 mm. Hg. If air is breathed, this combination of circumstances will reduce the arterial oxygen tension to 30 mm. Hg and the saturation to 45%. The inhalation of 30% oxygen, on the other hand, should restore the arterial oxygen tension to 75 mm. Hg and the saturation to 90%. At the present time all the Commonwealth Antarctic bases are virtually at sea-level. However, even at normal barometric pressure, the inhalation of 21% oxygen during anaesthesia would often lower the arterial point to the upper bend of the dissociation curve, leaving the patient with no reserve in the event of temporary respiratory obstruction —a contingency which must be anticipated. The value of an oxygen-enriched carrier gas would thus appear to outweigh the disadvantages of carrying cylinders of oxygen. The importance of oxygen is in inverse ratio to the skill and experience of the person administering the anaesthetic.

Since it is pointless to administer 100% oxygen, it remains to consider the other constituent of the carrier gas. The additional narcotic effect of 70% nitrous oxide in the presence of halothane would hardly justify the extra bulk and weight. There would seem to be no objection to nitrogen as the diluent gas, and it has been found practicable to entrain air by a small stream of oxygen and thereby attain a carrier gas containing 30% oxygen, with a very modest expenditure of cylinder oxygen. The percentage of oxygen will change relatively little with variation of the entrainment ratio from 1:5 to 1:9 (Table I). Contrary to the fears of Sir Hubert Wilkins, air collected at the South Pole was found to have the same composition as elsewhere (L. G. C. E. Pugh and J. M. Adam, personal communication).

TABLE I.—*Oxygen Percentage with Various Entrainment Ratios (Oxygen : Air)*

Entrainment ratio	1 : 4	1 : 5	1 : 6	1 : 7	1 : 8	1 : 9
Percentage oxygen in mixture ..	36·8	34·2	32·2	30·8	29·8	28·8

The Apparatus

Construction

British Oxygen Gases (Medical Division) undertook the construction of a prototype apparatus which appeared to meet the requirements (Figs. 1 and 2). A 72-gallon (325-litre) cylinder of oxygen was sufficient for an administration lasting five hours. Cylinder

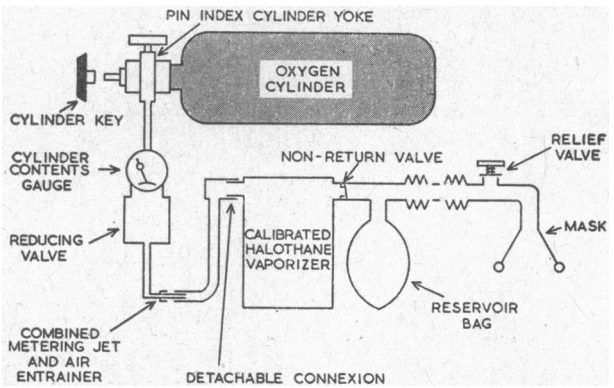

FIG. 1.—Block diagram of the apparatus.

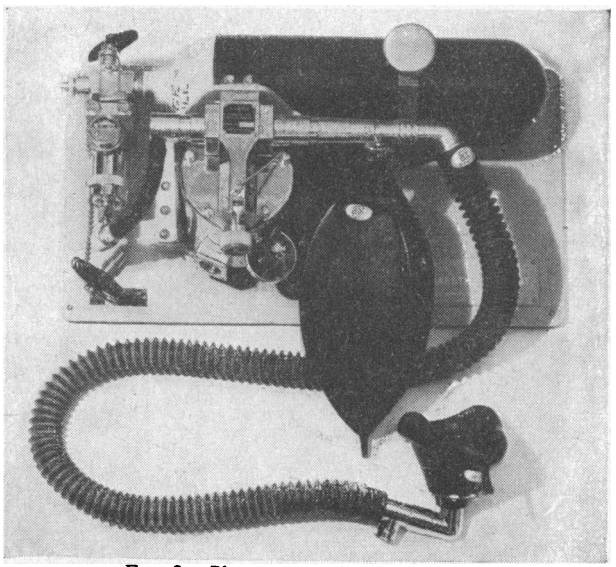

FIG. 2.—Photograph of the apparatus.

pressure was dropped across a miniature reducing valve to a level which resulted in a flow of 1 litre per minute through the metering orifice, which was also the jet of the air-entrainment device. This was designed to entrain 8 litres of air per minute against a back pressure of 1 cm. of water. The gas mixture (approximately 9 litres per minute of 30% oxygen) passed through a "fluotec" vaporizer (Mark I) to a conventional Magill breathing attachment. This attachment effectively prevents rebreathing provided that the fresh gas flow rate is in excess of the minute-volume of the patient (Mapleson, 1954; Woolmer and Lind, 1954). The minute-volume of an anaesthetized patient will seldom exceed 9 litres per minute (Nunn, 1958), but, should it do so, rebreathing will not reduce the *alveolar ventilation* below the fresh gas flow rates of 9 litres per minute (Mapleson, 1958).

It was decided to incorporate a non-return valve between the fluotec vaporizer and the Magill attachment. This conferred two advantages. Firstly, if a cylinder became exhausted the vaporizer could be disconnected from the entrainment device and the bag put out of circuit (tap not shown in Fig. 1). The patient could then draw air through the apparatus, exhaling through the relief valve. This would prevent interruption of the anaesthetic while changing cylinders. Secondly, short periods of manual ventilation would be possible by manual compression of the reservoir bag. Without the unidirectional valve this would drive gas to waste in the reverse direction through the air entry ports.

A higher oxygen flow rate and lower entrainment ratio are preferable at high altitudes, and a modification of the apparatus has been used to anaesthetize volunteers at a simulated altitude of 20,000 ft. (6,096 m.) (barometric pressure 349 mm. Hg).

Operation

The operation of the apparatus is similar to that of the conventional Boyle apparatus except that the composition and flow rate of the carrier gas are fixed. Once the cylinder is turned on, the carrier gas will flow until either the cylinder is empty or is turned off. The only adjustment possible is the concentration of halothane.

Since halothane vapour is not particularly irritant, the responsibilities of the person administering the anaesthetic may be reduced to the following: (1) ensuring a constant flow of carrier gas, (2) maintenance of an airtight seal between mask and face, (3) provision of a clear airway, and (4) regulation of the depth of anaesthesia by adjusting the concentration of halothane in the inspired gas. It is not impossible to instruct an intelligent layman to carry out the first three duties. An oropharyngeal airway is easily inserted under halothane anaesthesia, and it greatly simplifies the maintenance of the airway.

Regulation of the depth of anaesthesia is much easier with a calibrated vaporizer than with an open mask. Respiration is a satisfactory guide to depth of anaesthesia under halothane. Should respiration fail from too deep a level of anaesthesia, it may be expected to start again in due course when the halothane becomes redistributed and the arterial level falls. Mouth-to-mouth respiration may be conveniently practised during this interval, and it will at least ensure disconnexion from the supply of the anaesthetic (Cox, Woolmer, and Thomas, 1960).

It is unlikely that the surgeon or lay anaesthetist would detect hypotension due to decreased peripheral resistance, since the pulse would be easily felt and the appearance of the patient unchanged. Widespread experience of halothane anaesthesia suggests that this hazard is insignificant compared with other dangers of surgical intervention on an expedition.

Care and Maintenance

The apparatus requires no protection from extremes of temperature, other than prevention of condensation within the vaporizer. By obstructing the air-inflow ports the apparatus may be purged with dry gas from the cylinder. Immediately afterwards the face-piece mount should be connected to the vaporizer inlet to form a closed loop until required for use. It would, of course, be more economical to dry the apparatus with industrial oxygen, or with a blower fitted with a silica gel trap, should these be available. A silica gel trap might with advantage be left in the circuit during storage.

A simple test may be carried out to confirm that the total fresh gas flow is correct. If the face-mask connexion is obstructed and the cylinder turned on, the 2-litre reservoir bag should fill in 15 seconds. With the vaporizer set to zero and the reservoir bag disconnected from the circuit, a conscious subject may check the apparatus as a draw-through circuit. This will indicate whether the two valves are functioning correctly. At intervals, cylinder pressures should be checked for leakage and the rubber parts for deterioration.

Bottled halothane has a shelf life of at least three years, but it is probably inadvisable to leave it in the vaporizer for long periods after use. Excess liquid halothane may be drained off through the drain plug provided, but there will remain a considerable volume soaked up in the wick, which may be cleared by the following procedure: (*a*) Set the dial to maximum, open the drain valve, and remove the filler screw. Put a cork in the outlet. (*b*) Pass the carrier gas through until the smell of halothane disappears. This will take approximately 20 minutes.

Laboratory Trials

Cylinder Seal.—Leakage of oxygen from cylinders can be serious on an expedition (Hunt, 1953). In the past this has been due to the use of neoprene seals, which are unsatisfactory at low temperatures. In the present apparatus the cylinder valve is nylon to metal, and repeated cooling to −70° C. revealed no leakage, provided that the cylinder valve was closed with rather more than the customary force.

Reducing Valve and Metering Orifice.—The rate of gas flow from the metering orifice was measured by collection in a spirometer and studied at various cylinder pressures. The results (Table II) indicated that the flow was not significantly dependent upon cylinder pressure.

TABLE II.—*Effect of Cylinder Pressure on Gas-flow Rate*

Cylinder Pressure—Atmo.	Oxygen Flow Rate l./m. (ATPD)	Entrained Air Flow Rate l./m. (ATPD)	% Oxygen in Mixture
120	1·06	8·39	29·8
87	1·07	8·53	29·8
53	1·05	8·39	29·8
20	0·99	8·06	29·6

Air Entrainment Device.—Apart from geometrical design, the principal factor influencing entrainment ratio is back pressure. This was studied by metering the total flow of gas leaving the entrainment device against various levels of back pressure obtained by partial obstruction of the efferent tubing. It was found that a pressure of 5 cm. of water was sufficient to reverse the flow of air through the intake (Fig. 3). The entrainer was designed to work against a back pressure of 1 cm. of water, and it was thus necessary to keep the pressure-drop across the rest of the apparatus below this figure at the intended flow rate of 9 litres per minute.

Flow Resistance of the Apparatus.—The resistance of the total apparatus distal to the entrainer and with the fluotec set at 2% was less than 1 cm. of water at the designer's flow rate of 9 litres per minute (Fig. 4). Flow through the relief valve, however, is intermittent with peak flows of the order of 20–30 litres per minute. It was therefore important that this component should cause a pressure-drop relatively independent of flow. The normal Heidbrink valve is unsatisfactory in this respect (Nunn, 1958), and it was therefore modified by British Oxygen Gases, with the excellent results shown in Fig. 4.

Studies of the Mark II fluotec vaporizer (Fig. 5) showed that its resistance was not too high to preclude its use in a draw-through circuit.* When set to deliver 2% halothane the peak pressure-drop across it might amount to 2 cm. of water; but a recent study by Nunn and Ezi-Ashe (1961) has shown that this would have negligible effect upon ventilation.

Fluotec Vaporizer.—Mackay and Kalow (1958) and Hill (1958) have already shown that the accuracy of the calibration of the vaporizer is more than adequate for clinical requirements. We were therefore concerned only with its ability to withstand low temperatures. Messrs. Cyprane Ltd. kindly cooled a vaporizer to −70° C. for one week and, after rewarming, found the calibration to be unchanged. The entire anaesthetic apparatus was cycled between −50° C. and +50° C. four times by British Oxygen Gases Ltd. (Harlow) without the development of leaks or failures of gaskets. The fluotec vaporizers in Antarctica are in accord with Messrs. Cyprane's latest design principle, which prevents any possibility of the effluent gas containing halothane in excess of the maximum concentration shown on the dial.

Clinical Trials

There is abundant evidence that halothane in a non-narcotic carrier gas provides adequate anaesthesia for almost any surgical operation, its scope being similar to that of chloroform without the inherent dangers of the latter. The clinical trials were therefore concentrated on the ease and convenience of administration.

With the apparatus here described, some 70 patients were anaesthetized at the Whittington, Hammersmith, and Queen Alexandra Military Hospitals. Anaesthetics were administered by Colonel K. F. Stephens, Adviser in Anaesthetics to the Army, 12 registrar anaesthetists, 6 medical officers of the Falkland Islands Dependencies Survey, and the author for operations lasting from two minutes to two hours. Those participating who were anaesthetists already had considerable experience of halothane administered by conventional apparatus. Induction was with either thiopentone or halothane

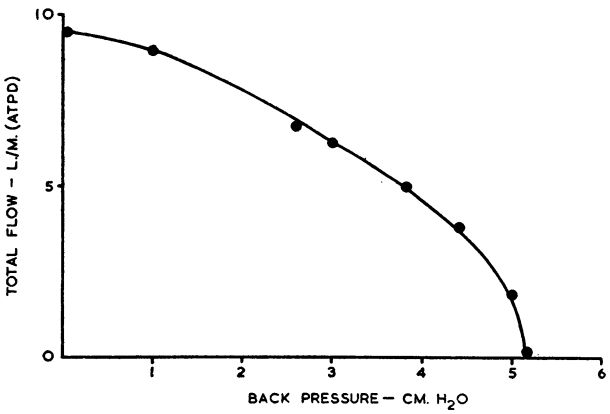

FIG. 3.—Total flow rate of gas leaving the entrainment device against the various levels of back pressure.

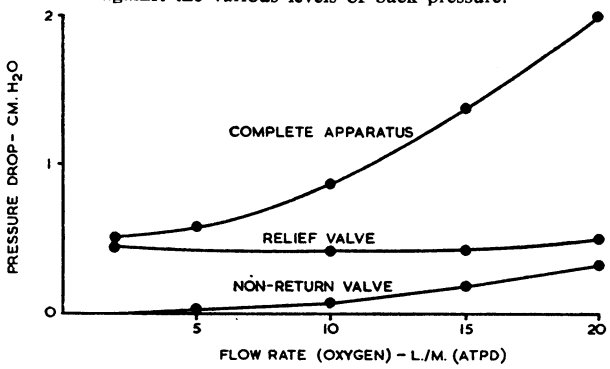

FIG. 4.—Flow-rate/pressure-drop characteristics of the entire apparatus with the valves separately shown. The vaporizer had been set to deliver 2% halothane.

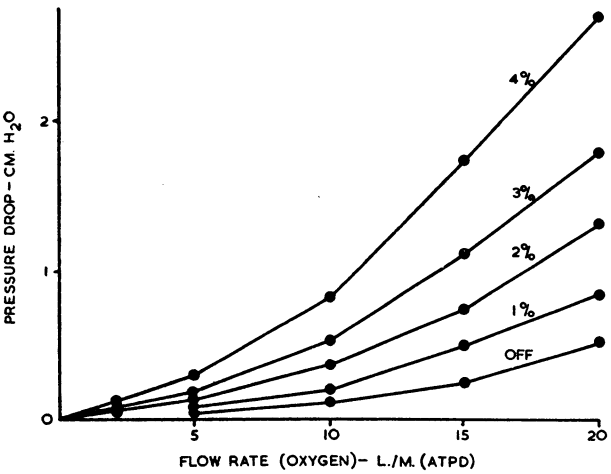

FIG. 5.—Flow-rate/pressure-drop characteristics of a Mark I fluotec vaporizer for various settings of the mixture control.

itself. To the out-patients no premedication was given, while in-patients received either papaveretum 20 mg. and hyoscine 0.4 mg. or pethidine 100 mg., promethazine 50 mg., and atropine 0.6 mg., given subcutaneously one hour preoperatively.†

Induction proved simple though slow. The vapour was not irritant and patients would tolerate 3% after a few breaths. In contrast to ether there was little excitement or disturbance of respiration. No patient required more than gentle restraint. The maintenance of the airway presented little problem and would be within the scope of a lay person acting under direction, particularly after the insertion of an oropharyngeal airway,

*The flow resistance of the Mark I vaporizer is not significantly different from that of the Mark II.

†We now prefer a premedication of pethidine 100 mg. and atropine 0.6 mg.

which was possible after about four minutes of the inhalation of 3% halothane. Induction of anaesthesia to a depth sufficient for skin incision required about eight minutes. This time could no doubt be reduced by using 4% halothane, but it appeared a useful safeguard for the apparatus to be unable to deliver a concentration in excess of 3%.

Recovery of reflexes at the end of operation was considerably slower than with nitrous oxide, but much depended upon the ability of the anaesthetist to anticipate the termination of the operation and discontinue the halothane.

There was, in general, no difficulty in obtaining sufficient relaxation for laparotomy. Many surgeons have now come to expect total paralysis for all surgical intervention in the abdomen, but, nevertheless, there would seem to be little doubt that 3% halothane would provide sufficient relaxation for appendicectomy or the suture of a perforated peptic ulcer. On an expedition a long induction and long recovery would be of less moment than in a general hospital with a busy operating schedule.

The most disquieting feature of halothane anaesthesia is the hypotension which is often seen, particularly in the deeper planes of anaesthesia. Systolic pressures down to 75 mm. Hg were encountered in the present study. Sequelae of hypotension due to halothane were not observed in this study nor when those participating have used halothane on other occasions. There is little experience of the use of halothane in the presence of surgical shock, but there is, as yet, no evidence to suggest that it is any more harmful than any other general anaesthetic agents. Wyman (1953) and Johnstone (1958) consider that vasodilatation is, in fact, beneficial—a view shared by many anaesthetists.

On a number of occasions the oxygen cylinder was removed during administration of an anaesthetic. The anaesthetist had no difficulty in converting the circuit to draw-through without interrupting the conduct of the anaesthetic, the use of air as carrier gas causing no visible change in the condition of the patient. A small number of patients were successfully ventilated artificially by manual compression of the reservoir bag. However, it is stressed that mouth-to-mouth respiration is preferable to this technique. Not only is the former technique difficult for the inexperienced, but, with the present apparatus, the fresh gas flow is interrupted during inspiration and thereby reduced to some 4–5 litres per minute.

At the present time medical officers appointed to the Falkland Islands Dependencies attend the Research Department of Anaesthetics of the Royal College of Surgeons for instruction in the maintenance of the apparatus. Thereafter they receive clinical instruction in its use at Hammersmith Hospital.

ADDENDUM.—Since this work was completed the author has made some use of the azeotropic mixture of halothane and ether as a general anaesthetic (Hudon, Jaques, and Boivin, 1958). Full evaluation of the mixture is not yet complete, but first impressions suggest that it might be more suitable than pure halothane under the conditions of an expedition. An equal depth of narcosis is obtained with a lower absolute concentration of halothane, and therefore the likelihood of hypotension is probably diminished. A calibrated and compensated vaporizer is available from Messrs. Cyprane for use with the azeotropic mixture.

I am grateful to Sir Vivian Fuchs and Dr. O. G. Edholm for their support in carrying out this work. We are indebted to the British Oxygen Gases development team at Harlow for the solution, at short notice, of the mechanical problems of the apparatus.

A production version of the apparatus (the "protothane") is under development by British Oxygen Gases Ltd.

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NITROGEN MUSTARD IN PALLIATION OF MALIGNANT EFFUSIONS

BY

V. B. LEVISON, F.F.R., D.M.R.T.

Consultant Radiotherapist, North Middlesex Hospital, London

A frequent and distressing complication of the late stages of disseminated malignant disease involving the serosa is the effusion of fluid into the pleural, pericardial, and peritoneal cavities. Little success attended the treatment of this until the introduction by Müller (1945) of the direct intracavitary injection of radioactive zinc (Zn-63) and subsequently radioactive colloidal gold (Au-198) (Müller, 1950). Treatment with Au-198 has certain inherent disadvantages, including the difficulty of handling it, but perhaps the most important of these is the radiation hazard involved to the medical and nursing personnel administering the treatment.

More recently attempts have been made to treat malignant effusions with chemotherapeutic agents, thus avoiding the radiation risk, using nitrogen mustard (HN2), thiotepa (Bateman, 1955), and mannomustine dihydrochloride ("degranol") (Sellei and Eckhardt, 1958). The series of cases described here were treated to assess the value of intracavity HN2 in the control of recurrent malignant effusions.

Present Investigation

Selection of Patients.—Initially all patients referred with recurrent effusions were accepted for treatment. Two patients (Cases 11 and 19) lived only a short time after the treatment, which may in fact have accelerated their death. Now only patients with a reasonable expectation of life and in fair general condition are accepted. Histological confirmation of the diagnosis was sought in all patients, but the pathology of the tumour was not considered as a basis for the acceptance or refusal of treatment.

Method of Treatment.—Most of the patients were admitted to hospital for three or four days. Two refused