ARTIFICIAL RESPIRATION

COMPARISON BETWEEN MANUAL AND INTERMITTENT POSITIVE-PRESSURE METHODS

BY

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The essential feature in the treatment of acute respiratory failure from any cause is adequate ventilation. Although the Schafer and, more particularly, the Holger Nielsen methods of manual artificial respiration are acceptable under most circumstances, there may be occasions when they are not practicable; for example, when there is injury to the chest or upper limbs, in confined surroundings, or when there is partial respiratory obstruction, such as that due to bronchospasm. It might therefore be desirable to have some other means of resuscitation that does not suffer from these limitations. The aim of this investigation was to examine the merits of intermittent positive-pressure ventilation as achieved by a modification of the classical mouth-to-mouth respiration, or by a simple hand-operated bellows resuscitator, and to compare it with the conventional Schafer and Holger Nielsen methods under similar conditions.

Methods

For obvious reasons it was not possible to investigate the efficiency of these forms of artificial respiration under field conditions, but a comparison could be made by ventilating anaesthetized, curarized subjects undergoing elective surgery. Fit patients between the ages of 20 and 40 years were selected. All were premedicated with "omnopon," 20 mg., scopolamine, 0.4 mg., and an amethocaine lollipop. They were induced with thiopentone, 0.75–1 g., and tubocurarine, 20–30 mg. A No. 10 Magill cuffed, endotracheal tube was inserted under direct vision to ensure a perfect airway. Anaesthesia and respiratory paralysis were maintained by the further administration of small doses of thiopentone and tubocurarine when necessary.

The efficacy of artificial respiration could not always be assessed from identical parameters. The oxyhaemoglobin content of the blood, using an ear oximeter, was determined in all the methods. Tidal volumes were measured by means of a spirometer in the manual methods. With mouth-to-mouth ventilation expired air was collected into previously vacuumized Barcroft tubes from a point at the mouth end of the endotracheal tube at the end of expiration and subsequently analysed.

Manual Methods

Ten subjects were placed face down on a sorbo-rubber mattress of 1½ in. (4 cm.) thickness laid on the floor. The patient's endotracheal tube was connected directly to a spirometer filled with air. Flow was so arranged that only normal air reached the patients, who were respired at 16 times a minute for five minutes by the Schafer method, followed by five minutes with the Holger Nielsen method. Care was taken to adhere in detail to the procedures laid down by the authors of the methods (Schafer, 1904; Nielsen, 1932).

Intermittent Positive-Pressure Methods

(1) The *mouth-to-mouth apparatus* consisted primarily of a standard light-type Service respirator worn by a donor. The respirator was slightly modified in that inside the facepiece a mouth-piece was fitted over the outlet valve and the nose of the valve was connected to a piece of corrugated tubing. The other end of this tubing was attached to an oronasal mask which could be held over the recipient's face. Valving was achieved manually by the donor closing a hole in the short connecting tube between the flexible hose and the oronasal mask during his exhalation (Fig. 1). Fourteen

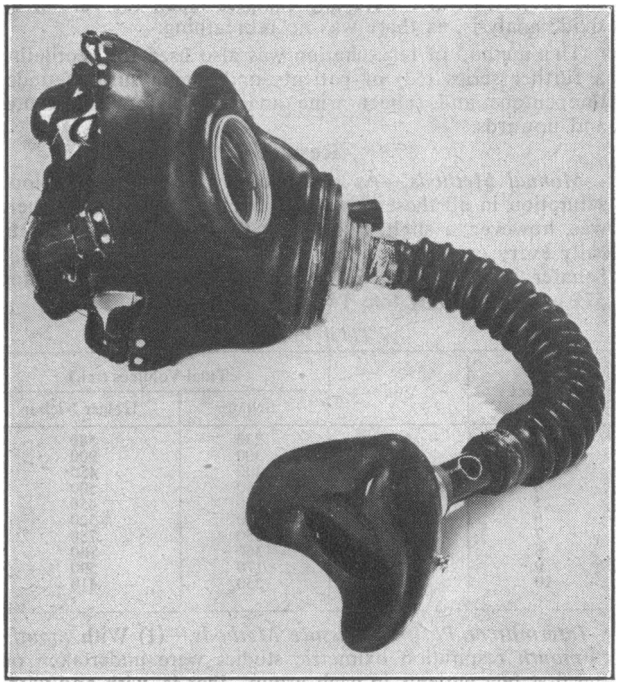

FIG. 1.—Photograph of mouth-to-mouth apparatus.

subjects were ventilated for 30 minutes by the same donor. On six occasions the apparatus was used as already described, and on the other eight occasions a carbon dioxide absorption canister was added, being placed between the outlet valve of the respirator and the corrugated tubing. All subjects were respired at 16 times a minute with moderate hyperventilation on the part of the donor. After the first few minutes this pattern of breathing could be maintained without any conscious effort. Gas samples of donor and recipient expired air were collected at five-minute intervals, the first being taken as soon as the endotracheal tube was in position.

(2) The *resuscitator* consisted of a bellows, maximum capacity 3 litres, and a face-mask, connected together by a dual purpose valve which permitted air to enter the face-mask and lungs during compression of the bellows, and allowed the subject's expired air to escape into the atmosphere during expansion, when air re-entered the bellows through a non-return valve under the back-plate. A relief valve, set to lift at 30 cm. of water, was also fixed under the back-plate. The mask and the bellows were so designed that the chin fitted into the mask, and when the bellows was operated the jaw was automatically held up, thus ensuring a clear airway (Fig. 2). Eight subjects were ventilated for five minutes, the mask being fitted over the face and not

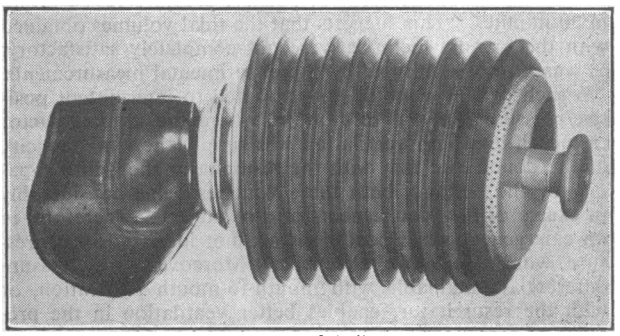

FIG. 2.—Photograph of bellows resuscitator.

connected directly to the endotracheal tube. The bellows was compressed at a rate of 16 times a minute and each stroke delivered a tidal volume of 2 litres of air, as calculated from the known volume of the bellows. It was not possible to measure the actual volume of air expired from the subject, neither were any samples taken for carbon dioxide analysis, as there was no rebreathing.

This method of resuscitation was also used for ventilating a further series (53) of patients undergoing surgery under thiopentone and tubocurarine anaesthesia for 30 minutes and upwards.

Results

Manual Methods.—As measured by oximetry, the blood saturation in all these subjects remained above 90%. There was, however, a slight fall during the experiment in practically every case. The mean tidal volumes obtained by the Schafer and Holger Nielsen methods were 262 ml. and 575 ml. respectively (see Table).

Tidal Volumes

Subject	Sex	Tidal Volumes (ml.)	
		Schafer	Holger Nielsen
1	M	230	580
2	F	300	900
3	M	200	450
4	F	350	500
5	F	240	450
6	F	170	320
7	F	350	750
8	F	360	800
9	F	170	590
10	F	250	410

Intermittent Positive-pressure Methods.—(1) With *mouth-to-mouth* respiration oximetric studies were undertaken on the first few patients in each group—that is, with and without the carbon dioxide absorber in the donor expired air circuit. As the oxygen saturation never dropped below 96%, oximetry was discontinued for the remainder of the experiments. The mean results of the carbon dioxide and oxygen concentrations of the expired air of the donor are shown in Fig. 3, and those of the recipient, with and without canister, in Fig. 4. With the canister the expired oxygen concentration of any patient did not fall below 14.15%, and the carbon dioxide did not rise above 5.7%. Without the canister the lowest expired oxygen concentration was 11.4%, and the highest carbon dioxide concentration 6.4%. (2) With the *bellows resuscitator* oximetry showed that no change occurred in the blood oxygen saturation of the eight subjects during the period of ventilation, and clinically there was no deterioration in their condition.

In the larger series ventilated by the bellows during surgery it was in no case possible to distinguish their clinical condition from that obtained with an ordinary, controlled respiration, anaesthetic technique.

Discussion

In this investigation all four forms of artificial respiration were found to be adequate for maintaining oxygenation of the anaesthetized, curarized subject under ideal conditions, but, whereas there was a slight fall-off in oxygen saturation with manual methods in five minutes, no such fall occurred with either form of positive-pressure resuscitation in 30 minutes. This suggests that the tidal volumes obtained with the manual methods were not completely satisfactory, as was in fact confirmed by the experimental measurements. No such deficiency could be attributed to intermittent positive-pressure artificial respiration, where the limiting factor in mouth-to-mouth ventilation was simply the vital capacity of the donor, and that with the resuscitator the 3-litre capacity of the bellows, both these volumes being considerably in excess of the requirements of any subject. Therefore, in an emergency, when conditions are not ideal, positive pressure would be more effective. Moreover, the pressure differential obtainable with mouth-to-mouth respiration, or with the resuscitator, enables better ventilation in the presence of respiratory obstruction, such as bronchospasm.

It has been argued, with little if any evidence, that positive-pressure ventilation inflates the stomach to the detriment of the lungs. There is evidence that this is not so at pressures up to 20 cm. of water (Mushin and Morton, 1958). Even if it were, a state of equilibrium would ultimately be reached in which both the lungs and the stomach would be ventilated. Positive-pressure respiration has also been criticized on the grounds of impairment of the venous return to the heart, but if the respiratory pressure is dropped to zero in between each breath venous return is not impeded, as judged by the absence of any change in mean venous pressure. The essential feature of any form of resuscitation is that the blood reaching the left side of the heart should be well oxygenated, even if the amount is a little reduced.

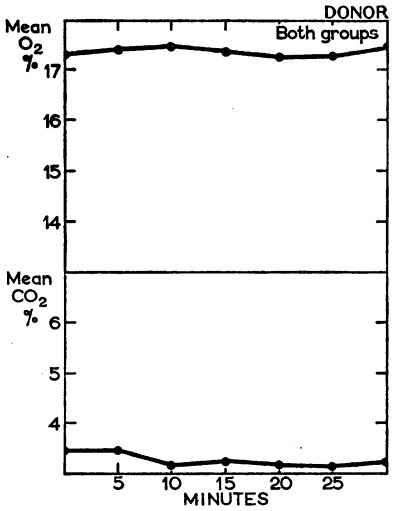

FIG. 3.—Mean carbon dioxide and oxygen concentration of expired air of donor.

In the two methods of intermittent positive - pressure respiration used in this investigation there was found to be little difference if the carbon-dioxide canister was included in the donor line of the mouth - to - mouth apparatus. When normal expired air was used the patients showed the typical clinical picture of respiratory acidosis under anaesthesia—namely, a flushed skin and a raised pulse rate and blood pressure — and needed an increased amount of barbiturate to maintain the same level of anaesthesia. Such a state has been shown by several authors to predispose to shock (Beecher and Murphy, 1950; Lucas and Milne, 1955). With a canister this form of resuscitation is satisfactory, but, in practice, any suitable canister would soon become exhausted and so replacements would have to be an integral part of the equipment. Apart from aesthetic considerations, an overall disadvantage of mouth-to-mouth ventilation is that there is a tendency on the part of the donor to overventilate, which must ultimately produce fatigue. The bellows resuscitator, on the other hand, has been shown to be entirely satisfactory: there are no components which have to be exchanged, fresh atmospheric air is used for each breath, there is minimal fatigue, and the complete apparatus is extremely simple.

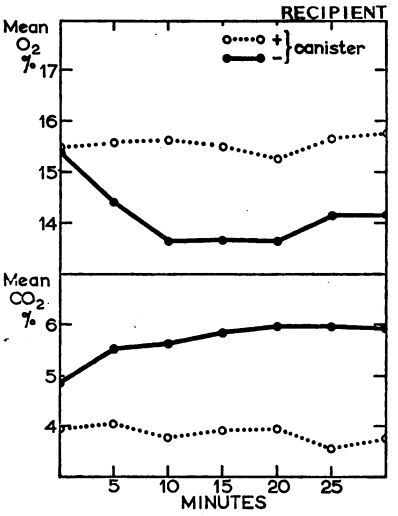

FIG. 4.—Mean carbon dioxide and oxygen concentration of expired air of recipient (with and without canister).

Summary

The relative merits of manual and intermittent positive-pressure artificial respiration have been investi-

gated in the unconscious, curarized subject. The Schafer and Holger Nielsen methods have been compared with mouth-to-mouth ventilation and a simple bellows resuscitator.

Manual methods have the advantage of requiring no apparatus, but they do require space. They are not so efficient for the oxygenation of the subject and may be relatively ineffective in the presence of bronchoconstriction.

Intermittent positive-pressure methods require apparatus, but are superior in terms of ventilation and oxygenation. The bellows resuscitator, a simple, compact apparatus, was still more efficient than the mouth-to-mouth apparatus.

The bellows resuscitator used in this investigation was designed and supplied by the Chemical Defence Experimental Establishment, Porton, Salisbury.

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CLINICAL EVALUATION OF "MIRADON"

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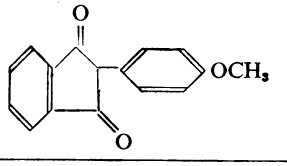
The value of anticoagulants in the treatment of certain thrombo-embolic conditions is now well established. Since the introduction of dicoumarol about 17 years ago (Butt *et al.*, 1941 ; Wright and Prandoni, 1942 ; Overman *et al.*, 1942), a number of hydroxycoumarin and indanedione derivatives, causing depression of the prothrombin activity of blood, have become available for use as anticoagulants. In addition to dicoumarol, these include ethyl biscoumacetate ("tromexan") (Tulloch and Gilchrist, 1951 ; Burke and Wright, 1951), phenindione ("dindevan") (Jaques *et al.*, 1950), phenylpropylhydroxycoumarin ("marcoumar") (Bourgain *et al.*, 1954), cyclocoumarol ("cumopyran") (Hanson *et al.*, 1951), and, more recently, warfarin (Clatanoff *et al.*, 1954) and nicoumalone ("sintrom") (Weiner *et al.*, 1956). They all suffer the disadvantage of being potentially dangerous and require frequent estimations of the prothrombin time for their control. As yet, however, they remain the best available drugs for treatment where prolongation of the prothrombin time is desired.

The purpose of this paper is to report the clinical trial of a new anticoagulant, 2-*p*-anisyl indanedione–1,3($C_{16}H_{12}O_3$), called "miradon" (anisindione). It appears to be more rapidly effective than and just as readily controlled as any anticoagulant in current use.

Material and Methods

Miradon has previously been tested in animals (P. L. Perlman and P. C. Giordano, unpublished work) without evidence of toxicity. It has the following chemical structure.



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Like phenindione, to which it is chemically related, miradon exercises its therapeutic action by depression of the prothrombin activity of the blood. In the presence of alkaline urine an orange colour is often detected, the result of katabolites of miradon.

Miradon was supplied in 50-mg. tablets for oral use, and the clinical trial was divided into three parts.

Part I.—A loading dose of 300 mg. was given to 12 healthy subjects, and the onset, rate, degree, and duration of prothrombin activity depression were recorded. None of these patients required anticoagulant therapy and all were free from known renal or hepatic disease. Estimations of the prothrombin time were performed according to the Quick one-stage method (Quick, 1942), using a phenol-saline preparation from human brain as a source of thromboplastin. Each batch of thromboplastin was diluted to obtain prothrombin % activation curves, and the results presented here are given as prothrombin % activity. The normal control using this method varied from 11 to 14 seconds. Prothrombin activity of 10 to 20% was regarded as a satisfactory therapeutic range ; this corresponds approximately to two to three times the normal plasma prothrombin time. Prothrombin activation curves were obtained for each patient.

Part II.—This constituted a therapeutic trial in 25 patients in whom anticoagulant therapy was thought to be necessary. These patients comprised 25 consecutive admissions who would otherwise have received therapy with another anticoagulant. Of these patients, 20 were suffering from a recent myocardial infarct, two from acute coronary insufficiency of increasing severity, two from deep venous thromboses of the legs (one of these had also suffered a pulmonary infarct), and one patient was given anticoagulant therapy while he received treatment to convert auricular fibrillation to normal rhythm. The aim in treatment was to maintain the prothrombin activity between 10 and 20%, and the dose for patients was ordered each day by the one observer. Estimations of the prothrombin time were performed before treatment began, 24 hours later, and thereafter daily between 9 and 10 a.m. for the first two weeks and for two out of every three days thereafter until treatment had been completed. During the course of this trial, random 24-hour periods were studied more closely to observe variations in prothrombin activity. The initial dose was 300 mg., except in three patients suffering from myocardial infarction in whom cardiac failure was present. (In these patients the initial dose given was 250 mg.) After 24 hours a further dose of 100 mg. was given, and thereafter the single daily dose depended upon the prothrombin times.

Part III.—The effect of oral vitamin K_1 on the prothrombin time was observed in a number of patients in whom "therapeutic levels" had been maintained for at least three days. The effect of vitamin K_1 was assessed further by the simultaneous oral administration of 20 mg. together with 300 mg. of miradon.

Results

Part I

In 11 of the 12 subjects given 300 mg. of miradon orally there was an effect upon the prothrombin time within six

Table I.—*Effect of a Loading Dose of* 300 *mg. of Miradon*

Subject	Duration of Effect (Hours)	Prothrombin % Activity at Start	Prothrombin Activity Less than 25% (Hours)	Maximum Effect	
				Prothrombin %	Time (Hours)
1	6–64	40	24–52	12	34
2	8–106	50	26–58	17	50
3	4–58	100	—	30	26
4	6–58	60	26–38	17	34
5	6–96	40	20–52	14	28
6	6–72	47	26–38	17	34
7	6–58	40	20–40	13	34
8	6–96	100	26–58	22	28
9	6–64	80	22–40	13	28
10	6–60	80	22–46	16	28
11	6–58	80	—	30	30
12	6–52	100	—	28	26