Fig. 5 shows actual changes in blood urea recorded during thiopentone/D-tubocurarine chloride/nitrous oxide/oxygen anaesthesia with manually controlled respiration. It can be seen from the results of seven cases investigated that the degree of hyperventilation that occurs during manually controlled respiration has a negligible effect on the blood urea, and in only one case was there any possibility of urea being incriminated as a cause of potentiation of thiopentone. It is interesting to note that in the one case in which a rise in urea was noted an excessive degree of hyperventilation was produced for investigational purposes. It would seem that with controlled respiration as carried out during anaesthesia there are no deleterious effects on kidney function and no marked rise in blood urea.

Loss of consciousness can follow hyperventilation if this is carried to extremes (McCance, 1935; Seevers *et al.*, 1939). A diminution in cerebral blood flow of the order of 30% (part of a general peripheral vasoconstriction) with an average increase of 15% in cerebral oxygen consumption has been reported (Kety and Schmidt, 1946). These would lead to a certain degree of cerebral anoxia, which may be aggravated by the effects of lowering the CO₂ tension on the oxygen dissociation curve of blood. While more oxygen can be taken up by the blood in the lungs, less will be given off to the tissues (Barach *et al.*, 1947). While it is known that potentiation of barbiturate anaesthesia can be accomplished by any means whereby central anoxia is produced (Peterson, Shideman, and Linares, 1950), this could not have played a part in the potentiation of thiopentone observed during manually controlled respiration. In these cases the degree of hyperventilation was so slight that none of the anaesthetists concerned realized that they were in fact hyperventilating the patients until they were told of the pH changes of the blood. Furthermore, using the thiopentone/D-tubocurarine chloride/nitrous oxide/oxygen sequence with manually controlled respiration of the same degree as in the series of cases referred to earlier, Prime and Gray (1952) found peripheral vasodilatation rather than vasoconstriction.

The fact that a patient is not breathing spontaneously will reduce the tone of the intercostals and hence abdominal muscles. If thiopentone/nitrous oxide/oxygen were used without a muscle relaxant, controlled respiration would reduce the amount of barbiturate required to produce satisfactory relaxation. This does not apply directly to the cases described above, but is the probable explanation of the lowered requirements of D-tubocurarine chloride observed at the end of two hours' anaesthesia with manually controlled respiration, as compared with patients who were allowed to breathe spontaneously.

All of the arguments quoted above are applicable to the anaesthetic technique described by Brennan (1952). With doses of 500 mg. of thiopentone for a large healthy adult he was able to produce long periods of narcosis. Undoubtedly he used a higher percentage of nitrous oxide (75%) to obtain a better analgesia, but it is doubtful if this actually resulted (Seevers *et al.*, 1937). Hyperventilation was purposely carried out from the beginning of the operation, and the changes in pH of the blood must have been greater than those recorded in either Fig. 2 or Fig. 4.

Conclusions

1. Subjects anaesthetized with thiopentone/D-tubocurarine chloride/nitrous oxide/oxygen require appreciably smaller amounts of barbiturate when respiration is manually controlled than subjects in whom respiration is aided or spontaneous.
2. More D-tubocurarine chloride is required for the first 45–60 minutes of the operation when respiration is controlled, but after two hours of anaesthesia requirements of relaxant are less than for subjects whose respiration is spontaneous or periodically aided.
3. With this sequence of drugs, aided or spontaneous respiration is accompanied by a fall in the pH of the

blood. Manually controlled respiration results in a rise in blood pH, indicating some degree of hyperventilation.

4. The changes in the pH of the blood, by affecting the distribution of thiopentone in the body, could account for conclusion 1.

5. Hyperventilation with oxygen prolongs the duration of thiopentone narcosis.

6. Other effects of hyperventilation which have been discussed are unlikely to have any potentiating effect on thiopentone.

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A NEW ARTIFICIAL RESPIRATOR

BY

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The increasing use of anaesthetic methods which involve complex intravenous techniques and the deliberate production of a state of apnoea have led to an interest in machines which are capable of ventilating a patient's lungs automatically and so restoring to the anaesthetist the freedom of his hands.

The respirator here described (Fig. 1) was designed for patients anaesthetized for thoracic surgery, and was first subjected to clinical trial at Aintree Hospital, Liverpool, in September, 1949. Since its introduction it has maintained respiration throughout the course of 538 major thoracic operations, of which 432 were cases of lung resection. That the trial has extended into what is, for this type of surgery, a long series of cases, speaks for the acceptance of the machine by surgeon and anaesthetist, and for the absence of complications that could be attributed to its use.

The respirator is of simple construction, the original model being built without special tools in a home workshop. Essentially the mechanism consists of:

1. A three-way tap by means of which the anaesthetic circuit can be connected to a hand-operated breathing-bag, or to a bag inside a glass bottle, at will.

FIG. 1.—Photograph of respirator.

2. A magnetically controlled valve which utilizes a flow of compressed air to build up and disperse an air pressure within the bottle, the alternating pressure cycle rhythmically compressing and releasing the breathing-bag and inflating and deflating the lungs. During deflation the compressed-air stream is used to create a venturi effect within the valve, the negative pressure produced being sufficient to overcome the inertia and resistances of the gas system and assist the pressure in the breathing-bag to return to the atmospheric level.

3. A device which enables the capacity of the system to be altered and permits the frequency of the respiratory cycle to be varied.

4. A self-regulating expiratory valve which allows any excess of anaesthetic gas to escape and ensures that the breathing-bag contains a constant volume of gas at the end of each expiration.

Provision is also made for varying the relative lengths of the inflationary and expiratory phases and for the retention of a positive pressure in the lungs throughout expiration if desired. Fig. 2 is a reproduction of one type of

FIG. 2.—A type of tracheal-pressure curve attainable with the machine.

tracheal-pressure curve which is attainable by ventilation with the machine. This follows closely the ideal form of curve described by Cournand *et al.* (1948). Should spontaneous respiration occur, the design of the valve makes it possible for the machine to respond to the resultant pressure changes and so follow the patient's respiratory pattern.

The rate of respiration may be adjusted within a range of 8 to 30 respirations a minute, and the pressure range available is from 5 to 25 cm. of water.

The water manometer used to record the pressure changes in the anaesthetic circuit also serves as a safety valve, the length of its tube limiting the inflation pressure that the machine can apply to 30 cm. of water. It is cut out of circuit when the three-way tap is turned to connect the patient to the hand-operated breathing-bag.

Features of the machine in use include simplicity of operation, a satisfactory performance at low inflation pressures,

the assistance given to deflation, and a "chattering" or increase in rate which gives audible warning (when the mechanism is suitably set) should an obstruction to respiration develop. The machine has been found to require very little attention in the way of maintenance, and the breathing-bag is easily removed for cleaning purposes.

Fig. 1 shows the appearance of the original apparatus, which is being developed and produced commercially by Medical and Industrial Equipment Ltd., London, under the name of the "Aintree respirator." A more detailed account of the machine may be found elsewhere (Esplen, 1952).

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THROMBOTIC MICROANGIOPATHIC HAEMOLYTIC ANAEMIA (THROMBOTIC MICROANGIOPATHY)

BY

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The condition described in this paper as thrombotic microangiopathy has attracted little attention outside the United States of America, where it is commonly known as thrombotic thrombocytopenic purpura. Clinically, the typical fully developed case presents a syndrome of fever, haemolytic anaemia, purpura, and fluctuating neurological disturbances; when this syndrome is present the diagnosis can be made at the bedside. Often, however, the most characteristic component of the syndrome, the *waxing and waning* neurological signs, appears only in the terminal stages of the illness; even in the earlier stages, however, identification by laboratory studies of the haemolytic nature of the anaemia and of the thrombocytopenia underlying the purpura should enable the diagnosis to be made, for the association of haemolytic anaemia and thrombocytopenic purpura is found in only a few conditions, most of which can be distinguished from thrombotic microangiopathy on other grounds. Unfortunately, the disease is not widely known and it is seldom considered in diagnosis: in most cases the correct diagnosis has first been made *post mortem*, by recognition of the pathognomonic disseminated lesions which occur only in vessels of microscopic calibre. No treatment has yet proved effective, and the disease has been fatal in all the recorded cases, usually within two to six weeks of its clinical onset. There are grounds for hoping that earlier diagnosis and treatment may lower the mortality. The following account of thrombotic microangiopathy is therefore presented, with a report of two new cases.

Historical

The first account of an undoubted example of this disease appears to have been given by Moschowitz (1924, 1925), who described a case of acute febrile haemolytic anaemia with petechiae and the development of neurological signs shortly before death; Libman is said to have recognized the condition clinically as a "new" disease. Histological examination *post mortem* showed hyaline thrombosis of terminal arterioles and capillaries. Moschowitz recognized that the wide dissemination of these lesions was unique; he thought that