phrenic. So far as treatment is concerned the more complex is the pattern and the longer it has persisted the more difficult will it be to treat, but if it is not too rigid and there is still a possibility of reorientation and reassociation with other mental processes recovery is possible. This is the state of affairs in the psychoneurotic, and by patient treatment of an analytical type, not necessarily by orthodox psycho-analysis, the pattern can be unravelled, the various components separated, and each given its proper value and time relations. In this way the pathological anxiety is resolved and the patient is restored to a reasonable sense of security.

In the psychotic schizophrenic, however, the pattern has, for some reason which is obscure, become extremely rigid and association with other mental processes has become very difficult or impossible; the patient has lost insight, and, having retired from reality into fantasy, is no longer particularly interested in being restored to security in relation to the real world. It would not appear that the explanation of this is wholly to be found in the intensity of the anxiety or the extreme degree of the insecurity; there would seem to be some other factor, possibly chemical, in the sense of cell or synapse integrity, which intervenes, but as to the nature of which we are ignorant. In such "closed" systems, however, psychotherapy is of very little avail, but modern convulsive therapy may afford relief by breaking them up, leaving the patient less anxious and less enclosed in his retreat from reality, but often at least more simple-minded and at a lower level of mental capacity.

Roizin (1939) showed that convulsive therapy produced small areas of cerebral necrosis, and these would interrupt and break up the facilitated "circulation" through the anxiety pattern.

Prevention of Pathological Anxiety

If pathological anxiety is to be prevented the manner in which the pattern is formed is important. At present our concern is with prevention under war conditions, both in the Services and in civil life. Ideally, it might be held, the way to prevent this condition is to exclude all those who owing to unfavourable circumstances in early life are potentially insecure. As a matter of fact, however, this is not only quite impracticable but would unnecessarily exclude a great number of people who could and would perform useful service even in positions of considerable danger. This is because, as we have seen from the example quoted, in the genesis of pathological anxiety not only is there a substratum of insecurity determined in the early years, but there is also a paucity of weapons wherewith the individual can maintain himself in the struggle for existence. The early conditions of our patient and her sister were probably very similar, but the patient later came to depend on her intelligence, and her intelligence alone, whereas her sister had many more strings to her bow. When her intelligence was threatened, then came the persistent anxiety, whereas in the case of her sister quite a lot of attributes would have had to be threatened before her feeling of security in life would have been seriously undermined.

Of course, if it is possible to recognize in time the individual who has been insecure in childhood, and also has in his own eyes too narrow an equipment with which to meet life, that person would be better evacuated from the danger area if he is a civilian or removed from the obligation of active general service if he is a combatant. Only occasionally, however, can such people be recognized in time for complete prevention of breakdown, but

after an individual has been subjected to strain, and is clearly showing signs of serious anxiety, his previous reactions to life should be carefully investigated. Not only the competent psychiatrist but also every understanding physician with even a little psychological knowledge will be able to appraise the situation and will see the wisdom of removing such a person as is described above from the strain of a continued feeling of insecurity before he has completely broken down into a useless liability to the nation and later a continuous burden on the taxpayer.

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MANAGEMENT OF RESPIRATORY DEPRESSION DURING ANAESTHESIA

BY

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The rapidly increasing use of the intravenously administered "light" barbiturates in modern anaesthesia has brought into greater prominence problems involving respiratory depression. All the barbiturates used in this way are apt to produce respiratory depression, particularly following heavy premedication; but if this disadvantage is realized, and is faced frankly by the modern anaesthetist and countered by appropriate measures, it presents no serious bar to the employment of a technique which is undoubtedly one of the outstanding advances of recent years in anaesthetics.

The barbiturate which seems to be generally acknowledged to produce by far the best results is sodium pentothal (Tovell and Thompson, 1936; Heard, 1936; Murphy, 1936; Mallinson, 1937), but it can also give rise to the most pronounced degree of respiratory depression, especially if not handled by an experienced administrator. Very occasionally—but much less frequently than its predecessor, evipan—pentothal causes severe laryngeal spasm, though this happening is usually due to errors of technique, such as too slow or too rapid a rate of injection. Evipan causes considerably less respiratory depression, but it is definitely inferior to pentothal in its effects and less reliable in its results. What follows here is therefore chiefly concerned with the use of pentothal as the intravenous agent.

Methods of Correcting Respiratory Depression

There are two chief ways to correct respiratory depression severe enough to cause anoxaemia, arising during anaesthesia.

1. STIMULATION OF THE RESPIRATORY CENTRE

This can be done by drugs injected or by carbon dioxide inhaled. The latter is useful in some circumstances and can if necessary be combined with the second method to be described; but it has its contraindications, particularly where the anaesthetic technique includes spinal analgesia (Mallinson, 1938). The most useful and reliable

drug up to date, particularly where barbiturates are concerned, despite the apparently conclusive theoretical arguments cited to prove its chemical and physiological inactivity, seems to be coramine. In practice it can almost be guaranteed to make a patient depressed by a barbiturate wake up enough to require restraint to prevent him falling off the table. It does, however, need to be given in sufficient dosage (5 c.cm. or more) and direct into the circulation. Picrotoxin is another recently suggested drug which has been used, especially in barbiturate poisoning (suicidal, etc.). It is stated to be a highly efficient cerebral and medullary stimulant in addition to its effect as an antagonist to barbiturate action (Kohn, Platt, and Saltmann, 1938). Not enough is as yet known about it to make any definite assessment of its place in anaesthetics. A number of other drugs, such as metrazol and cardiazol, are also used, but they do not appear to be as effective as coramine.

As a rule such drastic measures as those outlined above are not necessary.

2. INFLATING THE LUNGS WITH OXYGEN

Inflation a few times is all that should be necessary in the vast majority of cases unless a severe overdose of the barbiturate has been given. A source of oxygen under controlled pressure should always be available during the administration of an anaesthetic. It is now well understood that its presence is absolutely essential for safety when intravenous barbiturates are being used (Jarman and Abel, 1936; Jarman, 1939; Mallinson, 1937). Furthermore, it provides complete immunity from the dire effects of uncorrected respiratory depression, whatever the anaesthetic may be. It should be emphasized that "presence of oxygen under pressure" implies more than that it should be somewhere in the building: it must be literally *at hand*. It was with this in mind that the machine described below was designed.

The emergency oxygen button of a McKesson anaesthetic machine provides an ideal example of oxygen under controlled pressure, instantly available, and in hospital work, where the patient is usually anaesthetized in the theatre unit itself, is all that is needed. In nursing-home practice, however, conditions are apt to be very different. Most patients in these circumstances now expect to be rendered oblivious of all subsequent proceedings as rapidly as possible and before leaving their beds. A pentothal induction, for example, is ideal for this purpose, or avertin may have been ordered; but often it so happens that a maze of corridors and several floors separate the patient's room from the operating theatre. Sometimes the situation is rendered even more trying by the absence of a lift. In any case a somewhat anxious interval is liable to occur, starting after the induction and lasting throughout the journey along corridors and up or down in lifts till the operating theatre is reached, where the anaesthetist's McKesson has been set up. It is obviously impossible for even the most portable type of McKesson to accompany the patient on this journey, but an apparatus which embodies the principle of the direct oxygen supply found on that machine and without the anaesthetic parts of it solves the difficulty, and can be made quite light and portable.

The apparatus Messrs. A. Charles King have made for me (see Fig.) is of such a nature. It consists of a light wood and aluminium base on which is mounted a single thirty-gallon oxygen cylinder (C). Attached to this is a special type of reducing valve (V) having an adjustment (A) whereby the pressure reduction from the cylinder

pressure of 1,800 lb. per square inch can be varied from 5 lb. to 30 lb. per square inch. The maximum pressure obtainable from the emergency button of a McKesson is 60 lb. per square inch, and in practice even this is found to be perfectly safe when applied through a face-piece, because the face-piece will be lifted off the patient's nose and mouth by the pressure of the gas long before any harm can come to the respiratory system itself (McKesson, 1926); thus there is provided an automatic safety-valve action. If, however, the oxygen is being administered through the intratracheal tube direct, then it is wise to reduce considerably the maximum pressure available and to apply it with caution. The reducing valves provided on the average continuous-flow machine, on the other hand, deliver only at 5 lb. pressure, which, while perfectly adequate

C = Cylinder. V = Valve. A = Adjustment. G = Gauge.
P = Press-key. H = Handle.

when working through an intratracheal tube where there is an absolutely clear and unobstructed airway, may become quite insufficient to inflate the lungs through a face-piece in the presence of any perceptible degree of obstruction, and even when supplemented by squeezing the bag of the machine is totally useless in the presence of such obstruction as is produced by laryngeal spasm—and the manœuvre usually ends in the bag coming off the machine!

A gauge (G) shows the pressure in the cylinder, and hence provides a reliable indication of its contents; this is of considerable importance to the anaesthetist if he is to avoid being let down in an emergency by an almost empty cylinder. The apparatus is worked by a press-key (P) which allows oxygen to flow at the previously determined pressure only when it is held depressed. The oxygen is led thence through strong rubber tubing to the face-piece, which when not in use is held in a socket attached to the stand. A carrying handle (H) is provided, and the whole machine is protected by a canvas overall, thus making a small and compact little unit. The weight of the apparatus, including full cylinder (thirty-gallon), is approximately 14 lb. A fifteen-gallon cylinder can be used: it provides enough gas and considerably reduces the total weight; but this size is apparently not being made now for some obscure reason and is increasingly difficult to obtain. Alternatively, one of the new light metal cylinders can be fitted if expense is no object. The

over-all measurements (with thirty-gallon cylinder) are as follows: height, 19 inches; breadth, 9 inches; depth, 6 inches.

The Machine in Use

The compactness and lightness of the machine enable it to be carried with ease to the patient's room and placed alongside him on the locker or bedside table. After the patient is asleep and on the journey to the theatre the anaesthetist can take the apparatus along with him without being incommoded by a weighty and cumbersome anaesthetic machine, and with the comfortable feeling that should undue respiratory depression manifest itself during the journey it can be rapidly and easily countered on the spot. Should this need arise, the supply cock on the cylinder having been turned on, the face-piece is detached from its socket and applied to the patient's face firmly but without undue pressure. Next the control key is pressed for a second or two and then released, exactly as is the emergency button on a McKesson. By this means an artificial inspiration is produced and the lungs are inflated with oxygen. The face-piece is then lifted slightly and a natural expiration takes place. This manœuvre is repeated as often as is necessary at regularly spaced intervals of a few seconds each. As a rule two or three insufflations are all that is needed before every trace of cyanosis disappears and normal colour and function are restored.

The above apparatus is also very useful, and all that is required to be taken along, when a pure pentothal anaesthesia is decided upon, which nowadays seems to be the case on an increasing number of occasions. For such an anaesthesia a complex apparatus for the administration of nitrous oxide, ether, cyclopropane, etc., is unnecessary, and can safely be left in the car, thus avoiding the trouble and exertion inseparable from carting into the nursing home and setting up heavy anaesthetic machinery suitable for the administration of an inhalation anaesthetic. This question assumes really major importance in the absence of porters (which seems to be a regrettably frequent occurrence), especially if the day be hot and the anaesthetist late!

Conclusions

Pentothal is now generally agreed to be without appreciable effect on the heart (Mallinson, 1937; Pratt and others). Some workers, it is true, have described occasional irregularities on electrocardiographic investigation which do not appear to be of any great significance (Kohn and Lederer, 1938). Others, however, do not confirm this finding (Volpitto and Marangoni, 1938). The drug is nevertheless capable of producing considerable respiratory depression, especially after heavy premedication or excessive dosage; but it is only when the means to correct the resulting anoxaemia promptly and adequately are lacking that respiratory depression may bring in its train myocardial damage and cardiac failure, with the resultant collapse of the patient and all its attendant perils. If such means are at hand, and, what is more, in a form sufficiently light and easy to carry about, little fear of any major respiratory complication arising during anaesthesia need be felt.

Statistics with regard to intravenous anaesthesia now exceed 8,000,000 administrations (Jarman, 1939), and tend to show that this type of anaesthesia compares favourably with any other form, with the possible exception of gas-and-oxygen, in respect of mortality.

Finally it is claimed that the constant presence of a source of oxygen under controlled pressure during intra-

venous narcosis materially adds to the already excellent margin of safety possessed by this type of anaesthetic.

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THE VALUE OF INBRED MICE IN RELATION TO THE GENERAL STUDY OF MAMMARY CANCER

BY

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Much progress has been made in recent years in the elucidation of the mechanisms involved in the origin of mammary cancer. This is due largely to the availability of a number of inbred strains of mice in which the females exhibit a high tendency to the spontaneous development of this type of cancer. The value of such animals to the experimentalist lies in their short life-span and in the ease with which a large number of tumour-bearing animals can be obtained. Provided there is good evidence that the processes concerned with the high incidence of mammary cancer in these mice represent only an exaggerated form of the processes operating in widely outbred mice (which are comparable with human stock), then it is permissible to apply the results of such studies to the elucidation of the problem in the human subject.

Varying opinions have been expressed as to the relation between genetically pure strains and outbred mice. Cramer and Horning (1937) state that "there may be differences between the aetiology of mammary cancer in mice of mixed strains and those of specially inbred strains with an inherited high susceptibility to mammary cancer." The basis for this suggestion is their opinion that in outbred mice the condition is a local disease curable by operation, whereas in inbred mice it is a general disease with local manifestations and cannot be cured by operation. Gye (1937) supports this view and states that conclusions drawn from observations on inbred mice cannot be applied without reserve to cancer in normal mixed stocks.

Sampson Handley (1938) reported the history of a family of five sisters with a strong predisposition to breast cancer; three of them suffered from double primary carcinoma of the breast. He suggests that the history of this family recalls the high incidence of breast cancer in certain inbred strains of mice, and shows that surgical treatment was of value in spite of the strong constitutional predisposition. He also states that in his experience double primary breast carcinoma in the human being is not confined to cases in which the family predisposition is especially strong.