to provide statistically valid conclusions at this stage. We are conducting a comprehensive trial with dithiazanine, and hope to publish a further report in due course.

Our thanks are due to the nursing staff at Coldharbour Hospital for their care and observation of the patients under treatment. We are indebted to Mr. H. J. Attride, chief technician, County Laboratory, Dorchester, who personally carried out all the egg counts in the trial. We also thank Eli Lilly and Co. Ltd. for supplying the "telmid" tablets, which were specially obtained from America for this trial.

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STATUS EPILEPTICUS TREATED WITH D-TUBOCURARINE AND CONTROLLED RESPIRATION

BY

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Status epilepticus is a condition in which a series of convulsions occur with such rapidity that in the intervals between them the patient does not regain consciousness. Many authorities agree that the prognosis is poor. Ford (1944) states that where the seizures cannot be controlled signs of exhaustion appear. The temperature rises, respiration is laboured, and tachycardia with signs of circulatory failure becomes evident. The heart may be dilated and pulmonary oedema is often the cause of death.

Small and Woolf (1957) have described severe histological damage to the brain resulting from status epilepticus with respiratory obstruction, and have stressed the dangers of anoxia in this condition, especially in children. It is desirable, therefore, that considerable attention should be directed towards the control and management of the airway in this condition, especially where it does not rapidly respond to the routine forms of treatment. Modern anaesthetic techniques involving the use of muscle relaxants and controlled respiration have proved beneficial in cases of convulsions due to tetanus. That they may also be of value in status epilepticus is shown by the following case history.

Case History

A known epileptic girl aged 11 was admitted to Alder Hey Hospital in status epilepticus. The convulsions were generalized, and began an hour before admission. Intramuscular injections of paraldehyde, 4 ml., phenobarbitone sodium, 1 gr. (65 mg.), and hyoscine, 1/150 gr. (0.43 mg.)

failed to control the condition. In spite of oxygen therapy she became cyanosed, and in view of this the aid of the anaesthetic staff was requested.

On examination the child was convulsing and cyanotic, with poor air entry into all areas of the lungs. There was marked masseteric spasm, which prevented the removal of copious blood-stained secretions from the pharynx. The pulse was rapid and weak.

D-Tubocurarine, 15 mg., was injected intravenously, following which the jaw relaxed and the convulsions ceased. After pharyngeal suction, a No. 5 cuffed Magill endotracheal tube was inserted, the cuff inflated, and the tube connected to an anaesthetic machine from which a mixture of 50% nitrous oxide and oxygen was delivered at a flow of 6 litres a minute. Endotracheal toilet was performed and a considerable quantity of secretions removed from the air passages. A carbon-dioxide absorber was introduced into the circuit, and ventilation was maintained by means of a Fazakerly respirator (Esplen, 1956) for 45 minutes. On auscultation there was now good air entry into all areas of the lungs. Scattered crepitations were heard throughout. Soon after the arrest of the convulsions the pulse rate fell from 130 to 110 a minute. Similarly, the temperature fell towards normal after the institution of controlled respiration.

After an interval of 45 minutes, as the effects of the initial dose of relaxant decreased, it could be seen that the convulsions persisted in a modified form. Accordingly, a further 3 mg. of D-tubocurarine was injected intravenously. Controlled respiration was maintained for a further two hours, the patient being ventilated by hand at intervals in order to assess the degree of relaxation.

No further doses of relaxant were required. After three hours the convulsions appeared to have ceased and respiration was assisted manually as it gradually returned to normal.

When the tidal volume was seen to be adequate the supply of nitrous oxide was turned off. The child promptly awoke and coughed on the tube, which was removed after pharyngeal suction. She spoke quietly to the nurse before turning on her side and falling asleep.

The subsequent course was uneventful and she was discharged home.

Discussion

In the severe case of status epilepticus a state of respiratory insufficiency exists which must be relieved. Gaseous exchange is impaired by recurrent convulsions and by respiratory obstruction, while oxygen demand and metabolic rate are greatly increased by muscular hyperactivity. Heat production rises and the resultant pyrexia causes additional oxygen demand. If in addition there is a state of circulatory insufficiency and the heart is dilated, the use of drugs which markedly depress the myocardium would seem to be contra-indicated.

The method of treatment which was adopted in this case provides rapid relief from the state of respiratory insufficiency without the use of agents which add to the cardiac embarrassment. The convulsive irregular respiration of the epileptic state is replaced by controlled respiration. The adequacy of the airway is maintained by an endotracheal tube, and obstructing material in the respiratory passages is easily removed by suction. Trauma to the mouth, teeth, and tongue is avoided.

Both respiratory obstruction and hyperventilation may cause pulmonary oedema. It is known that positive-pressure respiration counters the tendency for an increased amount of fluid to leave the pulmonary capillaries. If, as Ford suggests, death frequently results from pulmonary oedema in this condition, the use of controlled ventilation should be beneficial.

Arrest of the muscular hyperactivity entailed by long-continued convulsions must greatly reduce metabolic rate and oxygen demand. Reference has been made elsewhere (Freier and his colleagues, 1957) to the cessation of sweating, fall in temperature, and slowing of the pulse rate which follow the use of muscle relaxants in convulsive states, and similar effects were noted in the case described above.

Phenobarbitone sodium and paraldehyde are perhaps the most commonly used agents in the treatment of this condition. There is agreement that in many cases they are effective, and that they possess a wide margin of safety. Where these fail to control the convulsions, ether or chloroform by inhalation, or thiopentone by intravenous injection, is often advised.

Diethyl ether may cause a significant degree of myocardial depression (Fisher, Bennett, and Allahwala, 1951). When administered without adequate premedication it results in a copious flow of secretions. Chloroform is noted for its harmful effect on the cardiac muscle and the conducting system of the heart. This latter effect is most likely to occur during induction where the level of circulating endogenous adrenaline is high, as is probably the case in status epilepticus. That thiopentone may cause a reduction in myocardial efficiency has been shown by Prime and Gray (1952). This effect is known to be pronounced in states of circulatory insufficiency. Furthermore, this agent has not the same degree of anti-convulsant activity as has phenobarbitone (Goodman and Gilman, 1955), and its effects may be transient.

Were a patient suffering from hypoxia, obstructed respiration, circulatory failure, pulmonary oedema, and cardiac dilatation being assessed for operation, it is unlikely that the modern anaesthetist would express a preference for such agents or techniques.

In contradistinction, D-tubocurarine has no marked effect on circulatory dynamics in normal dosage (Prime and Gray, 1952), and nitrous oxide is noted for its non-toxic properties. However, D-tubocurarine has no central anticonvulsant action, and should therefore be used in combination with an agent such as phenobarbitone.

Summary

The use of D-tubocurarine and controlled ventilation in a case of status epilepticus with marked respiratory embarrassment is described. Some advantages of this form of treatment are briefly discussed.

I am indebted to Dr. T. Cecil Gray, Dr. G. Jackson Rees, and Dr. Alan L. Stead for criticism and advice in the preparation of this paper, and to Dr. F. P. Hudson for permission to treat the case.

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DIPHTHERIA PROPHYLAXIS

LONG-TERM EFFICIENCY OF SEPARATE AND COMBINED ANTIGENS ADMINISTERED EARLY IN LIFE

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We have previously reported the comparative efficiency of two clinical procedures where infants received their first injection at 3 months of age and were bled at 15 months of age and their diphtheria antitoxin titres measured (Spiller *et al.*, 1955). The two clinical procedures were: (a) three monthly inoculations of *Haemophilus pertussis* vaccine, followed by two 0.5-ml. doses of P.T.A.P.—the separate group; and (b) three monthly inoculations of combined fluid diphtheria toxoid (30 Lf per dose) with *H. pertussis* vaccine—the combined group. It was found that the geometric mean titre of antitoxin following the separate group was high at 0.883 u./ml. and that the titre following the use of combined prophylactic was also high but not as high as from the P.T.A.P., being 0.54 u./ml. Responses from A.P.T. measured under roughly similar conditions was 0.27 u./ml. (Barr *et al.*, 1950). From this it was concluded that nothing serious was lost in the use of the combined antigen when three doses are given and "alum" is not employed, and that there was much to be gained.

A number of these same children, now 4½–5 years of age, have been bled again and the sera assayed for their diphtheria antitoxin titre. The figures obtained, together with each child's titre at 15 months of age, are shown in the Table.

In the first bleeding—some 7–10 months after the last inoculation in the primary immunization course—there were 81 infants in the combined group and 79 in the separate group. In this present study, some 4–4½ years after the end of the primary immunization course, we obtained 25 sera from the combined group and 28 from the separate group.

As each child was known, it was possible to make individual comparisons and to calculate the geometric mean titres of these two present groups when the members were 15 months of age. Any discrepancy between these latter values and the original total group means would be an index of lack of random sampling. It will be seen from the Table that there would appear to be a discrepancy; in both cases the geometric means of the present two groups when measured at age 15 months are greater than those of the entire groups at 15 months of age: 0.902 u./ml. against 0.883 for the separate group, and 0.80 against 0.54 for the combined