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.

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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

group. The former is obviously not significant. When, however, the appropriate test is applied to the latter (t-test on logs of titres) the resulting value $P=0.4$ is obtained, indicating no lack of randomness in the children bled the second time in this group.

The geometric mean titre of those children some $4\frac{1}{2}$ years after the end of their course of primary immunization (see Table) is much greater than might have been expected. The two mean titres, of almost equal value, 0.112 and 0.131 u./ml. represent a drop of about one-seventh in the interval of three years (15 months to $4\frac{1}{2}$ -5 years) and demonstrate that

*Diphtheria Antitoxin Titres of Children, at $4\frac{1}{2}$ -5 Years of Age, Who Received Their Primary Course of Immunization at 3-7 Months of Age. "Separate" Group Received Three Monthly Doses of *H. pertussis* Vaccine Followed by Two 0.5 ml. Doses of P.T.A.P. "Combined" Group Received Three Monthly Doses of Combined Fluid Diphtheria Toxoid With Pertussis Vaccine. (i)=Child's Antitoxin Titre at 15 Months of Age; (ii)=Same Child's Antitoxin Titre at $4\frac{1}{2}$ -5 Years of Age in u./ml. of serum*

"Separate" Group		"Combined" Group	
(i)	(ii)	(i)	(ii)
2	0.5-1.0	1.25	0.1-0.2
0.8	0.02-0.05	1.25	0.1-0.2
1.25	0.1-0.2	1.25	0.1-0.2
0.8	0.05	1.25	0.5
1.25	0.2-0.5	0.8	0.05-0.1
4	0.05-0.1	3.0	1
1.5	0.2-0.5	0.5	0.02-0.05
0.1	0.02-0.05	0.8	0.02-0.05
0.8	0.2-0.5	0.8	0.2-0.5
2.0	0.1-0.2	0.3	0.2-0.5
2.0	0.05-0.1	0.8	0.1-0.2
0.3	0.1	0.9	0.2-0.5
2.0	0.05-0.1	0.3	0.02-0.05
3.0	0.2-0.5	1.0	0.02-0.05
0.8	0.1-0.2	0.3	0.1
1.25	0.2-0.5	1.25	0.05-0.1
1.25	0.1-0.2	3.5	0.5-1.0
0.3	0.02-0.05	0.3	0.05
0.125	0.01-0.02	0.3	0.1-0.2
1.5	0.5-1.0	0.8	0.1
0.3	0.05-0.1	2.0	0.5-1.0
1.25	0.05-0.1	0.6	0.1-0.2
2.0	0.1-0.2	1.25	0.2-0.5
1.25	0.1-0.2	2.0	0.5
0.8	0.2-0.5	0.1	0.002-0.005
0.2	0.02		
1.25	0.1-0.2		
0.6	0.05		
n=28		25	
Geometric mean, 0.902	0.112	0.800	0.131
s.d., 0.401	0.443	0.358	0.563
Geometric mean of original group of 79 infants, 0.883		Geometric mean of original group of 81 infants, 0.541	

immunization in early infancy with either two doses of P.T.A.P. or three of combined toxoid and vaccine is a remarkably efficient procedure. It is calculated that a geometric mean titre, in a group, of 0.13 u./ml. of antitoxin indicates a 99% Schick-negative reaction rate in that group (Holt, 1955). And over and above this it may be pointed out that every infant was well primed—namely, made a good response to the primary course of immunization (Spiller *et al.*, 1955) and would react rapidly to any trace of toxin due to an incipient diphtheria infection.

Bousfield (1957), who used almost identical reagents as a triple prophylactic for similarly aged infants retested over exactly the same interval of time, found 9 out of 148 such children Schick-positive—a Schick-negative rate of 93.9%.

Nevertheless, because the antitoxin response to diphtheria toxoid (plain)—pertussis mixtures may not be uniformly great, possibly due to variations in the

adjuvant properties of different batches of vaccine (Bousfield and Holt, 1957; Holt, 1957), it is to be recommended that children who have been given combined prophylactic in early infancy should receive the usual pre-school booster of fluid toxoid or of fluid toxoid and tetanus toxoid if they had received a primary immunization course of both diphtheria and tetanus toxoid.

Summary

The antitoxin titres of children who had received a course of primary immunization against diphtheria, by either of two clinical procedures, were measured at ages 15 months and $4\frac{1}{2}$ -5 years.

At age 15 months the geometric mean titre of diphtheria antitoxin from three doses of *H. pertussis* vaccine followed by two of P.T.A.P. was 0.88 u./ml. of serum, and that from three doses of combined fluid diphtheria toxoid with *H. pertussis* vaccine was 0.54 u./ml. At $4\frac{1}{2}$ -5 years of age there is no significant difference between the two means—0.112 u./ml. for the former and 0.13 u./ml. for the latter—which are eminently satisfactory.

Nevertheless, despite these satisfactory results it is recommended that children who have been given combined antigens in early infancy be given a booster dose of toxoid at pre-school entry age. This is because it has been found that the primary responses to combined fluid toxoid and vaccine are not uniformly good.

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William Heinemann Medical Books, Ltd., have published a series of five books on sex education, written by Marion O. Lerrigo and Helen Southard in consultation with Dr. M. J. E. Senn. *Parents' Privilege* is intended to advise parents what they should tell children of up to 8 years old about anatomy, conception, and birth. *A Story About You*, for boys and girls in the 9-12-year age group, describes the physical differences between men and women and the changes which occur at puberty, and explains the act of mating. *What's Happening to Me?* provides for teenagers a fuller discussion of physical, mental, and emotional changes which take place during adolescence, with some account of ovulation, fertilization, and birth. *Learning about Love* is a frank discussion of sex problems which may arise among young people from 16 to 20 years of age. *Sex Facts and Attitudes* discusses the physical and emotional aspects of sex, and briefly explains the reproductive system, conception, prenatal development, and birth, for the guidance of those responsible for the sex education of children and adolescents. Each book contains about 64 pages and some coloured drawings and diagrams, and costs about 7s. 6d.