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The influence of suxamethonium on cardiovascular and respiratory function in the anaesthetized horse

P. LEES AND W. D. TAVERNOR

Departments of Physiology and Surgery, The Royal Veterinary College Field Station, Hawkshead Lane, North Mimms, Hatfield, Hertfordshire

1. In horses anaesthetized with halothane the intravenous administration of suxamethonium chloride, at a dose level of 0·2 mg/kg, produced a short-lived period of hypoventilation, which was associated with increases in arterial blood P_{CO_2} levels and in plasma concentrations of bicarbonate, sodium and potassium ions, and reductions in arterial blood pH and P_{O_2} values.

2. The respiratory depressant action of suxamethonium chloride 0·2 mg/kg was accompanied by increases in blood pressure and heart rate. Doses of suxamethonium chloride 0·4 mg/kg produced similar but quantitatively greater changes in cardiovascular and respiratory function. These effects were not accompanied by cardiac arrhythmias, with the exception of one animal, in which an unusually prolonged period of apnoea occurred.

3. The cardiovascular effects of suxamethonium during halothane anaesthesia were diminished but not abolished when the respiratory depressant action of suxamethonium was prevented by applying positive pressure ventilation.

4. The cardiovascular effects of suxamethonium in horses anaesthetized with halothane were partially antagonized by propranolol and completely antagonized by hexamethonium. It is suggested that the cardiovascular effects of suxamethonium are mediated by two distinct mechanisms: reflexly mediated increases in heart rate and sympathetic vasoconstrictor tone due to the respiratory depression, and a direct stimulant action of suxamethonium on peripheral, autonomic ganglia.

5. Much less pronounced changes in cardiovascular function, but not in respiratory function, were recorded when suxamethonium was administered to horses anaesthetized with ether.

6. A slight degree of tachyphylaxis to the cardiovascular and respiratory effects of suxamethonium was recorded in horses anaesthetized with halothane.

7. Some atypical effects of suxamethonium on respiration are described.

The reported side effects of suxamethonium in laboratory animals include tachycardia, bradycardia and changes, usually of a pressor nature, in mean arterial blood pressure. In addition, cardiac arrhythmias have also been recorded following the administration of suxamethonium to monkeys, cats, dogs and rabbits (Adams & Hall, 1962 ; Beretervide, 1955 ; Bourne, Collier & Somers, 1952 ; Bovet, Bovet-Nitti,

Guarino, Longo, Fusco & Marotta, 1949 ; Conway, 1961 ; Dowdy & Fabian, 1963 ; Galindo & Davis, 1962 ; Purpura & Grundfest, 1956 ; Stevenson, 1960a, b ; Thesleff, 1952). Alterations in cardiovascular function in response to suxamethonium have also been reported in man, cardiac arrhythmias occurring particularly in children (Barreto, 1960 ; Craythorne, Turndorf & Dripps, 1960 ; Dentan & Vourc'h, 1967 ; Dowdy & Fabian, 1963 ; Graf, Ström & Wåhlin, 1963 ; Leigh, McCoy, Belton & Lewis, 1957 ; Lupprian & Churchill-Davidson, 1960 ; Telford & Keats, 1957 ; Williams, Deutsch, Linde, Bullough & Dripps, 1961). It has been suggested that these cardiovascular effects are attributable solely to a temporary depression, or abolition, of respiration resulting from the neuromuscular blocking actions of suxamethonium (Hansson, 1958). On the other hand, other investigators, who have studied the effects of suxamethonium under conditions of controlled respiration, have suggested that the drug exerts a direct stimulant action on autonomic ganglia and increases the secretion of catecholamines from the adrenal medulla (Adams & Hall, 1962 ; Beretervide, 1955 ; Conway, 1961 ; Dentan & Vourc'h, 1967 ; Stevenson, 1960a, b ; Thesleff, 1952 ; Williams *et al.*, 1961).

Suxamethonium has been used in the horse in conjunction with general anaesthetics, and has also been administered to conscious animals, following which a pronounced tachycardia is produced together with cardiac arrhythmias (Hofmeyr, 1960 ; Neal & Wright, 1959 ; Tavernor, 1959, 1960). The object of the present investigation has been to examine the effects of suxamethonium on cardiovascular and respiratory function in the horse during general anaesthesia. The effects of the drug were recorded both in the presence and absence of controlled respiration and also before and after the administration of drugs which block the conduction of impulses across peripheral, autonomic, synaptic junctions.

Methods

Twenty-nine experiments were performed in horses ranging in weight from 191 to 512 kg and from 18 months to 15 years of age. No pre-anaesthetic medication was given in any experiment. In each case anaesthesia was induced by the rapid intravenous injection of thiopentone sodium at a dose rate of 10 mg/kg body weight, followed by endotracheal intubation and maintenance with either a halothane/oxygen or ether/oxygen mixture administered in a closed circle anaesthetic circuit.

The rebreathing bag was replaced by a spirometer, into which was incorporated a soda lime cannister for carbon dioxide absorption. Anaesthesia was maintained in a steady state by a constant inflow of a small volume of oxygen and anaesthetic agent into the spirometer.

When anaesthesia had been stabilized, a carotid artery was exposed and cannulated, the cannula being connected to a mercury manometer. Heparin was injected into the cannula as necessary but the animal was not heparinized. The zero pressure was taken from the level of the apex of the heart, the carotid artery pressure and the excursions of the spirometer being recorded on a kymograph. Respiratory tidal and minute volumes were measured with a gas meter, which was incorporated into the expiratory side of the anaesthetic circuit. Heart rate and rhythm were monitored with a Devices electrocardiograph using lead II limb electrodes.

Arterial blood samples were drawn anaerobically from a polythene cannula inserted into a carotid artery, the samples being taken at regular intervals in

heparinized, glass syringes. The syringes were capped, and if not analysed immediately they were placed in an iced container at 0° C. Oxygen tensions were measured with a Clarke oxygen electrode, and carbon dioxide tensions by either the equilibration technique described by Siggaard Anderson (1964), or using a direct reading Severinghaus electrode. Arterial blood pH levels were monitored with a Radiometer pH meter and micro-electrode system. The measurements of pH, P_{CO_2} and P_{O_2} were made either immediately or, for the samples stored in ice, within 4 hr of collection. The arterial plasma concentrations of sodium and potassium ions were measured with an EEL flame photometer, and plasma chloride was estimated by potentiometric titration with silver nitrate.

All the drugs used in this study were dissolved in normal saline and injected into a jugular vein. Suxamethonium chloride was administered at dose levels of 0·2 and 0·4 mg/kg (0·146 and 0·292 mg cation respectively) utilizing a solution containing 50 mg/ml. Hexamethonium bromide was given at a dose level of 10 mg/kg, using a 100 mg/ml. solution. Doses of 0·1 and 0·5 mg/kg of propranolol hydrochloride were administered as a 10 mg/ml. solution. The drugs were given by rapid intravenous injection, with the exception of hexamethonium, which was administered by slow intravenous infusion over a period of 10 min.

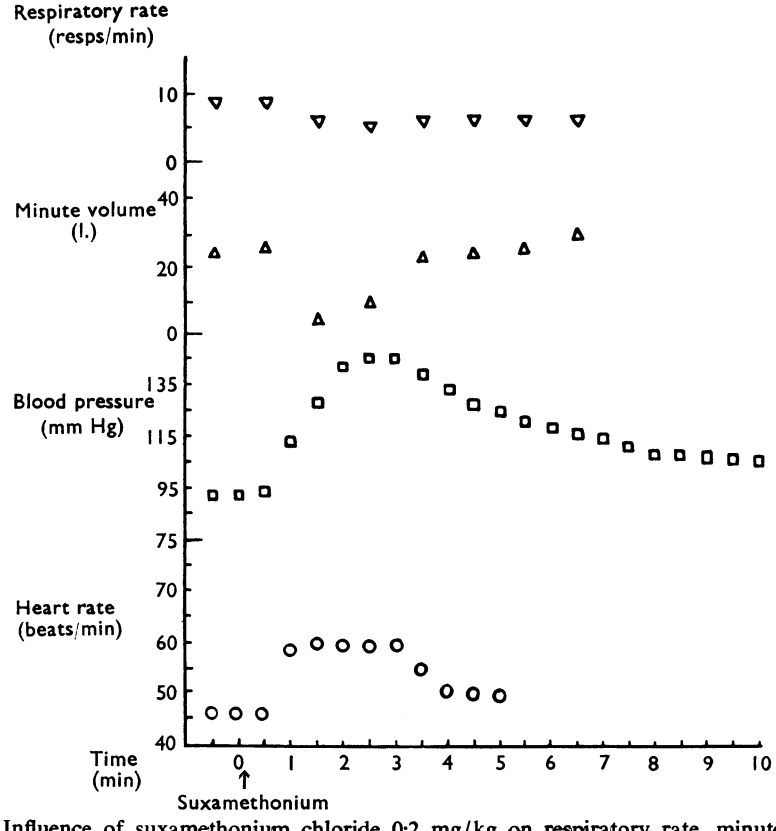

FIG. 1. Influence of suxamethonium chloride 0·2 mg/kg on respiratory rate, minute volume, blood pressure and heart rate of horses anaesthetized with halothane. Each point represents the mean value for nine experiments.

Results

Effects of suxamethonium during halothane anaesthesia

Following the intravenous administration of suxamethonium chloride 0·2 mg/kg, heart rate and blood pressure were elevated in each experiment (Fig. 1). These effects were usually manifest within 1 min of the injection of the drug, the tachycardia reaching a maximal value at a mean time of 1 min 42 sec after the injection and the peak of the pressure response being attained at a mean time of 2 min 54 sec after administration of the drug. The pressor effect was associated with a reduction in pulse pressure, this parameter returning to normal values within 2–4 min. In most instances the heart rate had returned to control values within 5 min of the injection of suxamethonium, whilst the pressor response returned to the pre-injection control levels more slowly. In every experiment, however, the blood pressure had returned to the pre-injection value within 12 min.

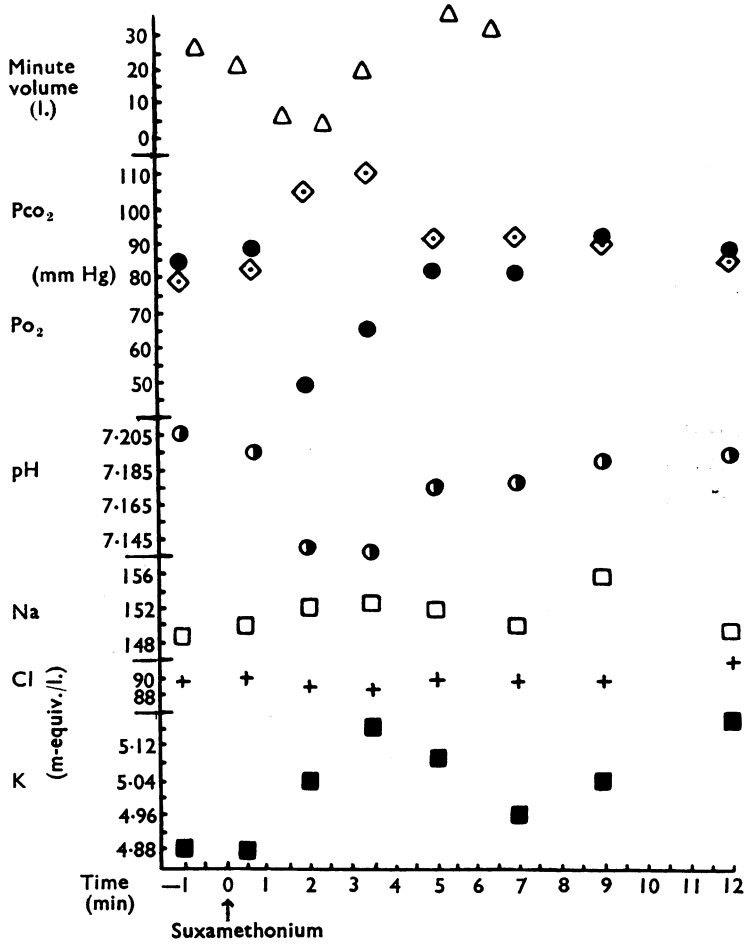

FIG. 2. Influence of suxamethonium chloride 0·2 mg/kg on minute volume (△), arterial blood P_{CO_2} (◈), P_{O_2} (●) and pH (◑) values, and plasma concentrations of sodium (□), chloride (+) and potassium (■) ions in horses anaesthetized with halothane. Each point represents the mean value for six experiments.

The cardiovascular responses were accompanied by a short period of hypoventilation, and in some experiments by a period of apnoea, which was usually less than 1 min in duration. This was followed normally by a mild, compensatory phase of hyperventilation (this response was obscured in Fig. 1 by taking mean values), after which the minute volume returned to control levels within 3–6 minutes of the injection of suxamethonium. The reduction in respiratory minute volume led to an enhancement of the moderate respiratory acidosis, which existed before suxamethonium was administered. The rise in arterial blood P_{CO_2} level and the depression of blood P_{O_2} and pH were greatest in the samples taken at 2 and 3·5 min after injection. The mean values of P_{O_2}, P_{CO_2} and pH for six experiments are illustrated in Fig. 2, from which it can be seen that these values had almost returned to normal within 5 min of administration of suxamethonium but did not finally return to control levels until the nine minute blood sample. The plasma concentrations of sodium, potassium and chloride ions are also shown in Fig. 2. There was a small, insignificant reduction in plasma chloride levels and the calculated values for base excess remained unchanged. The concentrations of sodium and potassium showed mean rises of 4·2% ($P<0·05$) and 5·7% ($P<0·05$) respectively. The mean plasma potassium concentration, having returned almost to the control level, showed a secondary rise of 5·9% ($0·05>P<0·1$) in the final, 12 min, blood sample.

In three experiments suxamethonium chloride was given intravenously at the higher dose level of 0·4 mg/kg, this dose producing qualitatively similar changes in cardiovascular and respiratory function to those recorded at the lower dose rate of 0·2 mg/kg. The depressant effect of suxamethonium on minute volume, however, was more prolonged at the higher dose level. In addition, the pressor and positive chronotropic responses to suxamethonium were greater than those occurring at the lower dose level (Table 1).

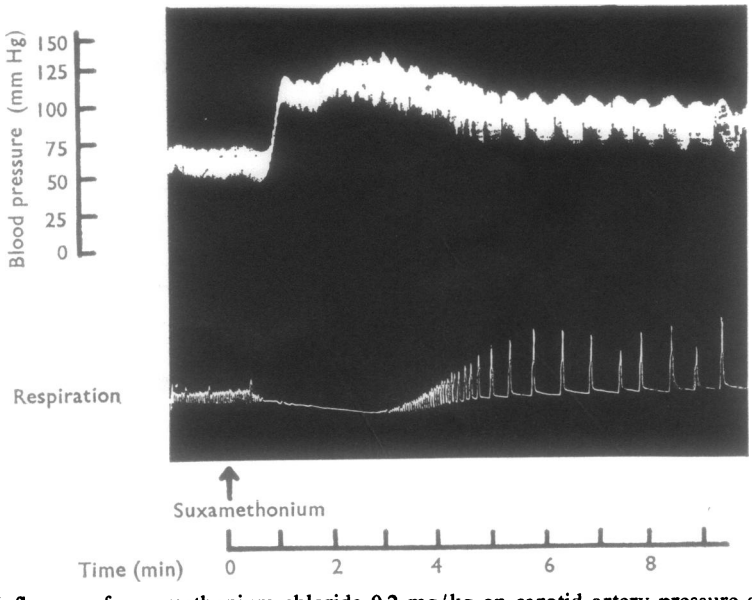

FIG. 3. Influence of suxamethonium chloride 0·2 mg/kg on carotid artery pressure and respiration of a 300 kg horse anaesthetized with halothane.

TABLE 1. *Influence of suxamethonium on cardiovascular and respiratory function in the horse*

Series	Number of experiments	Dose of suxamethonium (mg/kg)	Anaesthetic	Average maximal increase in heart rate (beats/min)	*P*	Average maximal increase in blood pressure (mm Hg)	*P*	Average maximal reduction in minute volume (l./min)	*P*
	9	0·2	Halothane	19·3±3·6	<0·001	57·9± 5·9	<0·001	19·7± 3·5	<0·001
A	3	0·2	Ether	3·3±2·4	>0·20, <0·30	14·3± 2·6†	>0·02, <0·05	26·6± 4·2	>0·02, <0·05
	3	0·4	Halothane	21·0±4·4	>0·02, <0·05	75·3± 7·1†	>0·001, <0·01	19·5± 6·6	>0·05, <0·10
	3*	(a) 0·2		19·3±2·9	>0·02, <0·05	58·3± 3·8	>0·001, <0 01	17·9± 9·3	<0·10, <0·20
B		(b) 0·2	Halothane	16·0±3·5†	>0 02, <0·05	46·7± 2·4	>0·001, <0·01	18·1±11·5	>0·20, <0·30
		(c) 0·2		12·7±4·1†	>0·05, <0·10	43·7± 7·5	>0·02, <0·05	19·4± 5·7	>0·05, <0·10
		(d) 0·2		12·7±4·1†	>0·05, <0·10	49·3± 6·5	>0 02, <0 05	20·9± 6·3	>0 05, <0·10
C	2**	(a) 0·2	Halothane	32·0±4·0	>0·05, <0·10	64·0± 6·0	>0·05, <0·10		
		(b) 0·2		21·0±3·0	>0·05, <0·10	27·5± 7·5	>0·10, <0 20		
D	3***	(a) 0·2	Halothane	8·7±2·4	>0·05, <0·10	47·3±13·5	>0·05, <0·10	26·4± 6·5	>0·05, <0·10
		(b) 0·2		1·3±1·3†	>0·40, <0·50	3·0± 3·2	>0·40, <0·50	35·9±14·9	>0·10, <0·20
E	6****	(a) 0·2	Halothane	17·0±4·1	>0·001, <0·01	58·0± 5·1	<0·001	29·0± 8·1	>0·01, <0·02
		(b) 0·2		8·7±1·9	>0 001, <0·01	35·0± 6·7†	>0·001, <0·01	30·8± 7·7	>0·01, <0·02

Suxamethonium was administered in all cases by rapid intravenous injection.
The results are mean values±S.E. The statistical significance of each value was determined by *t* tests, the appropriate values of *P* being given.

† Indicates a significant difference between the value and the first value in each of the series A–E ($P<0·05$).
* Effects of four successive doses (a–d) of suxamethonium administered at 12·5 min intervals.
** Effects of suxamethonium with (b) and without (a) controlled respiration.
*** Effects of suxamethonium before (a) and after (b) the administration of 10 mg/kg hexamethonium bromide.
**** Effects of suxamethonium before (a) and after (b) the administration of 0·1 mg/kg propranolol hydrochloride.

Two further points emerged from this series of experiments. First, in two animals which were in a relatively deep plane of anaesthesia, in contrast to the other animals in this series, suxamethonium produced an atypical effect on respiration (Fig. 3). In both animals respirations were rapid and shallow and mean arterial blood pressures were lower than normal (68 and 82 mm Hg respectively) before the administration of suxamethonium. In each experiment the injection of suxamethonium 0·2 mg/kg produced the usual short period of hypoventilation and a subsequent return of the minute volume towards control levels. The nature of the respiratory pattern then changed abruptly, the tidal volume showing a threefold increase and the respiratory rate decreasing to approximately two respirations per minute. This type of breathing continued in both animals for periods of 27 and 22 min, respectively.

Second, in all the horses in this series the injection of suxamethonium was followed by a moderate sinus tachycardia but cardiac arrhythmias were not observed in the lead II electrocardiographic recording. In addition, one animal, in which an

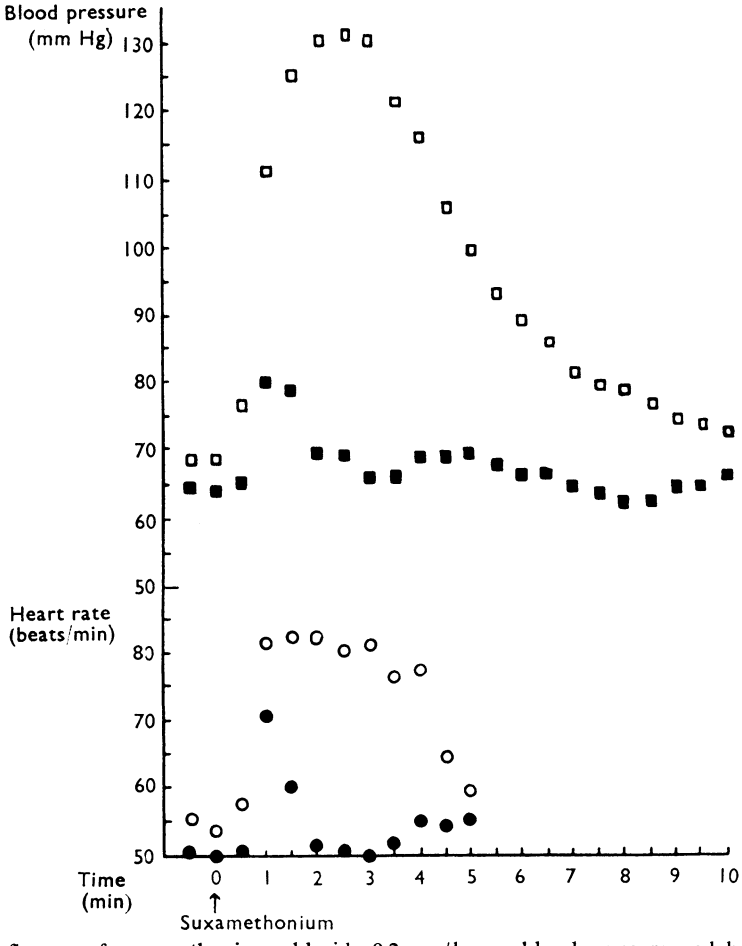

FIG. 4. Influence of suxamethonium chloride 0·2 mg/kg on blood pressure and heart rate of horses anaesthetized with halothane, before (□, ○) and during (■, ●) controlled ventilation. Each point represents the mean value for two horses.

unusually prolonged period of apnoea of 3·5 min duration followed the injection of suxamethonium, showed an initial tachycardia which was replaced after 3 min by a pronounced bradycardia. This bradycardia was associated with a wandering pacemaker followed by periods of sinus arrest, the heart beats occurring in groups of two or three, interspersed with short periods of arrest. Subsequently, the return of

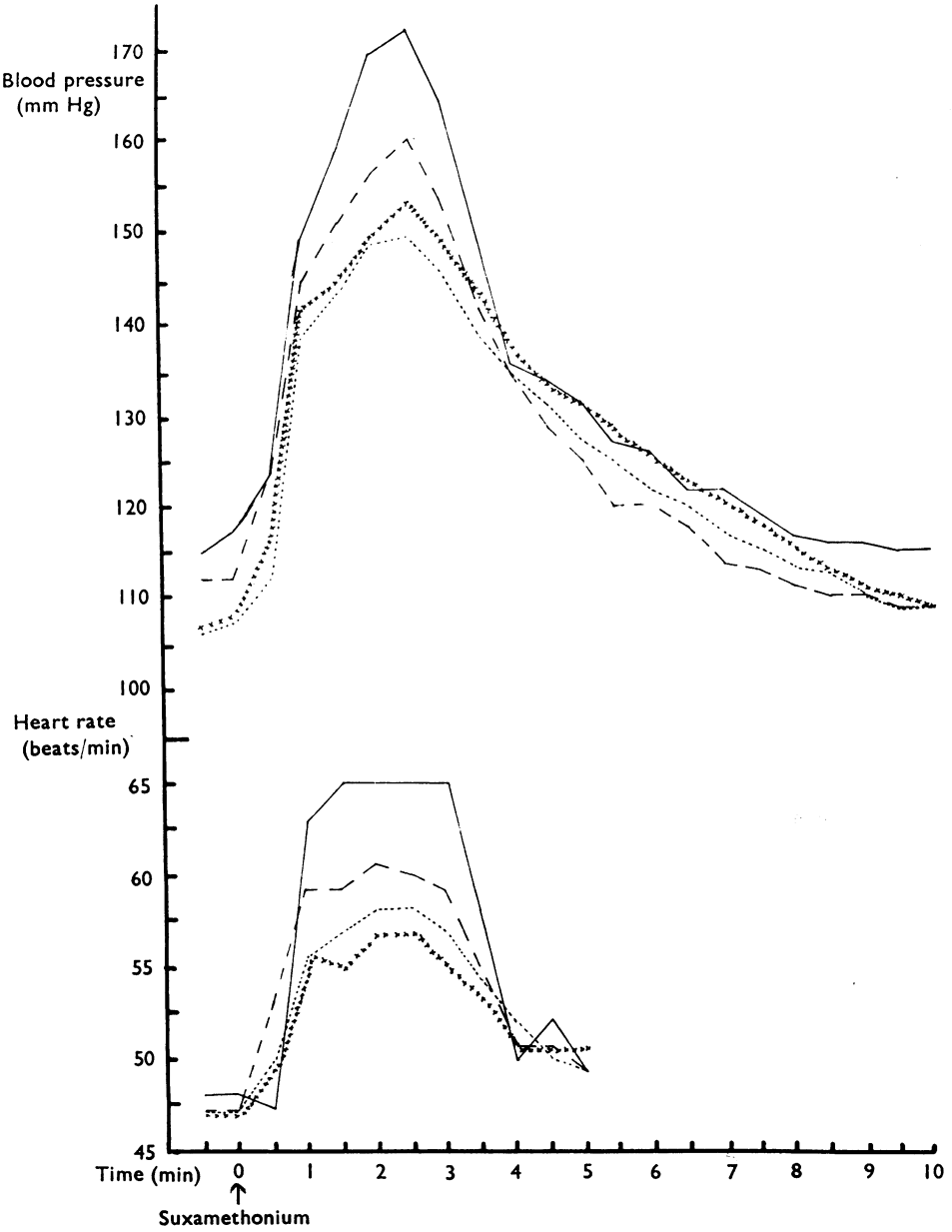

FIG. 5. Influence of suxamethonium chloride 0·2 mg/kg on blood pressure and heart rate of horses anaesthetized with halothane. Four successive doses of suxamethonium were administered at 12·5 min intervals, each line representing the mean values for three experiments. ——, first dose ; — — —, second dose ; - - - - -, third dose ; × × × ×, fourth dose.

normal breathing was accompanied by a steady increase of heart rate to the pre-injection levels and a return to normal rhythm. A second dose of suxamethonium produced similar changes in cardiovascular and respiratory function in the same horse.

Experiments with positive pressure ventilation

The effects of suxamethonium on cardiovascular and respiratory function were investigated both with and without the maintenance of control levels of respiratory rate and tidal volume using positive pressure ventilation. The mean results of these experiments are illustrated in Fig. 4, which shows that the positive chronotropic and pressor responses were greatly reduced when positive pressure ventilation was employed. The smaller increases in blood pressure and heart rate, which followed the administration of suxamethonium during controlled ventilation, were apparent in less than one minute and had returned to pre-injection levels within three mins. Following the return of these cardiovascular parameters to normal control levels, further slight increases in heart rate and blood pressure were occasionally recorded.

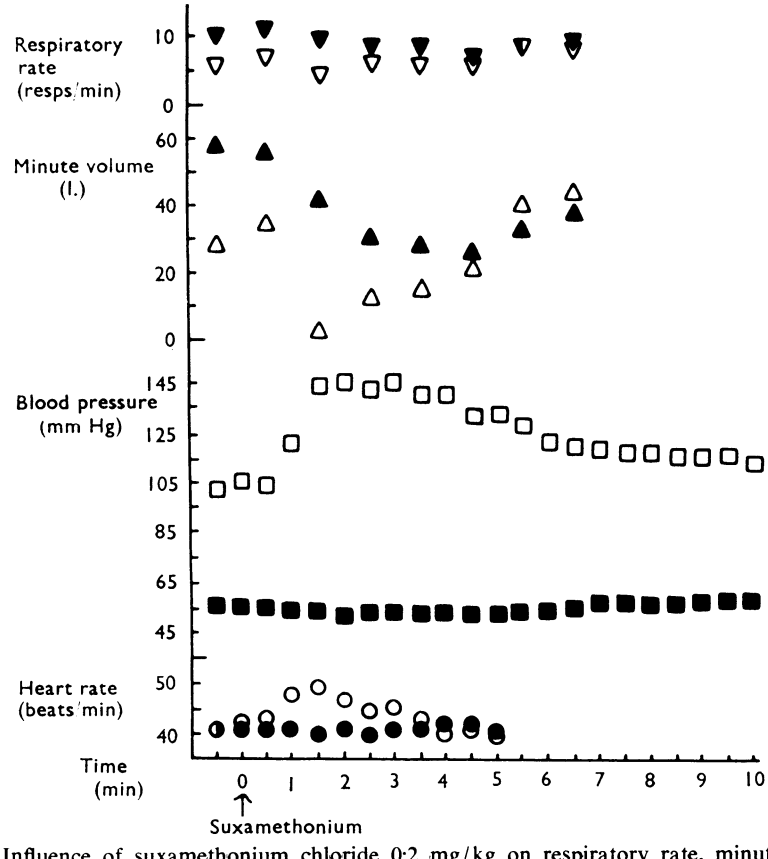

FIG. 6. Influence of suxamethonium chloride 0·2 mg/kg on respiratory rate, minute volume, blood pressure and heart rate of horses anaesthetized with halothane, before (▽, △, □, ○) and after (▼, ▲, ■, ●) the administration of hexamethonium bromide 10 mg/kg. Each point represents the mean value for three experiments.

Effects of successive doses of suxamethonium

The effects on cardiovascular and respiratory parameters of four successive doses of suxamethonium 0·2 mg/kg, administered at 12·5 min intervals, were investigated in three horses (Fig. 5 ; Table 1). The purpose of these experiments was twofold ; to determine first whether the responses to suxamethonium exhibited tachyphylaxis and second whether cardiac arrhythmias would occur after the administration of several doses of suxamethonium. Although the experiments gave no evidence of cardiac arrhythmias, a slight degree of tachyphylaxis did occur ; the increase in heart rate being significantly diminished following the second and subsequent doses of suxamethonium, the tachyphylaxis increasing with successive doses. On the other hand, the pressor response to suxamethonium was less pronounced with the second dose but was not further decreased with the third and fourth doses of the drug. Similarly, the maximal reduction in minute volume was slightly less pronounced with the second, compared with the first dose of suxamethonium, but was not further diminished with the third and fourth doses. The tachyphylaxis to the pressor and respiratory responses was not statistically significant.

Influence of autonomic blocking agents on the responses to suxamethonium

The responses to doses of suxamethonium 0·2 mg/kg given both before and after the administration of the autonomic blocking drugs, propranolol and hexamethonium, were investigated. Positive pressure ventilation was not used. The mean results of the experiments using the ganglion blocking drug, hexamethonium, are shown in Fig. 6 and a typical tracing is shown in Fig. 7. It is clear that the effect of suxamethonium on heart rate was abolished and the pressor action was also antagonized. In fact, the blood pressure occasionally fell slightly when suxamethonium was given after hexamethonium. Hexamethonium reduced slightly but did not abolish the resipratory depressant action of suxamethonium (Fig. 7).

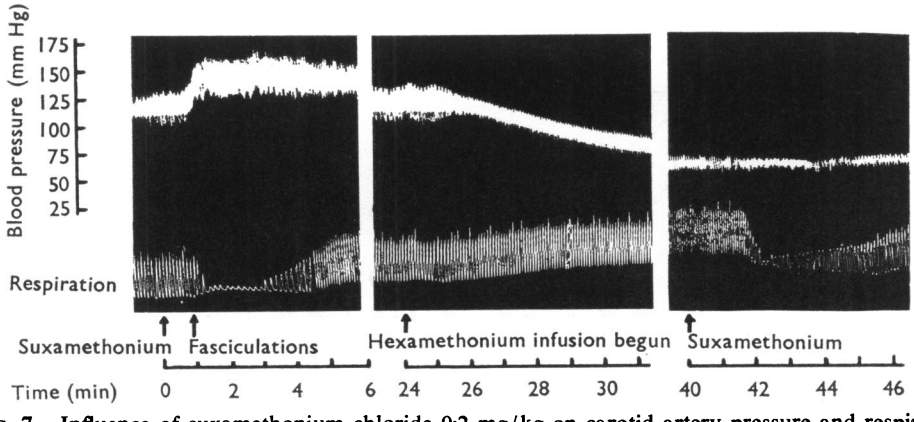

FIG. 7. Influence of suxamethonium chloride 0·2 mg/kg on carotid artery pressure and respiration of a 512 kg horse anaesthetized with halothane, before and after the administration of hexamethonium bromide 10 mg/kg.

The influence of the β-receptor blocking agent, propranolol, on the cardiovascular and respiratory responses to suxamethonium is shown in Fig. 8. The positive chronotropic and pressor responses to suxamethonium were reduced in magnitude, but in no experiment were they abolished. This reduction was greater than that occurring in the experiments where successive doses of suxamethonium were administered in order to measure tachyphylaxis. It is therefore unlikely that the partial antagonism of the cardiovascular responses to suxamethonium produced by propranolol could be ascribed wholly to tachyphylaxis to suxamethonium. The difference between the tachyphylactic response and the responses before and after propranolol were however, not statistically significant. Propranolol did not modify significantly the maximal respiratory depression produced by suxamethonium, although the duration of this effect was shortened in some experiments (Table 1).

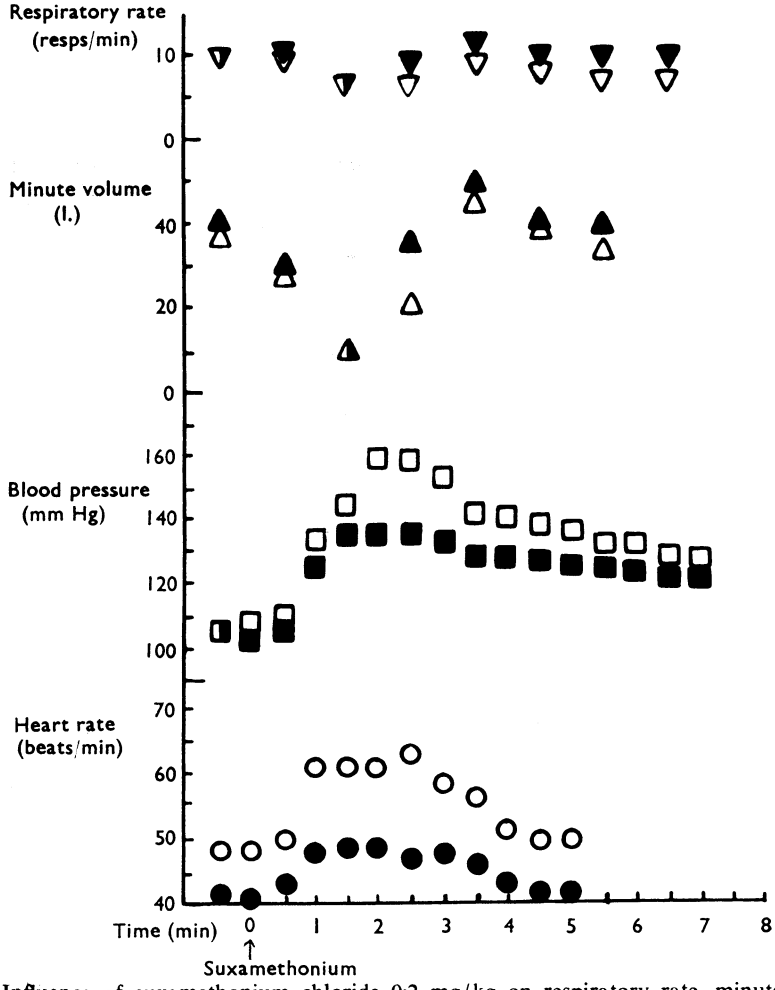

FIG. 8. Influence of suxamethonium chloride 0·2 mg/kg on respiratory rate, minute volume, blood pressure and heart rate of horses anaesthetized with halothane, before (▽, △, □, ○) and after (▼, ▲, ■, ●) the administration of propranolol hydrochloride 0·1 mg/kg. Each point represents the mean value for six experiments.

Effects of suxamethonium during ether anaesthesia

Suxamethonium was given at a dose level of 0·2 mg/kg to three horses under di-ethyl ether anaesthesia. Much smaller changes in heart rate and blood pressure were produced in these three animals than the changes observed during halothane anaesthesia (Fig. 9 ; Table 1). In the experiments under ether, suxamethonium produced an initial small rise in blood pressure, and this was followed by a more prolonged depressor phase. By contrast, the changes in heart rate were more variable ; in one instance a mild tachycardia was recorded, whereas in two other experiments the heart rate did not vary by more than 5% from the control levels.

Discussion

Many investigators have recorded changes in cardiovascular function following the administration of suxamethonium to man and laboratory animals. In some reports it is not clear whether the investigations were performed with controlled respiration or in animals breathing spontaneously. In addition, pre-anaesthetic medication with either atropine, phenothiazine derivatives or other drugs may have

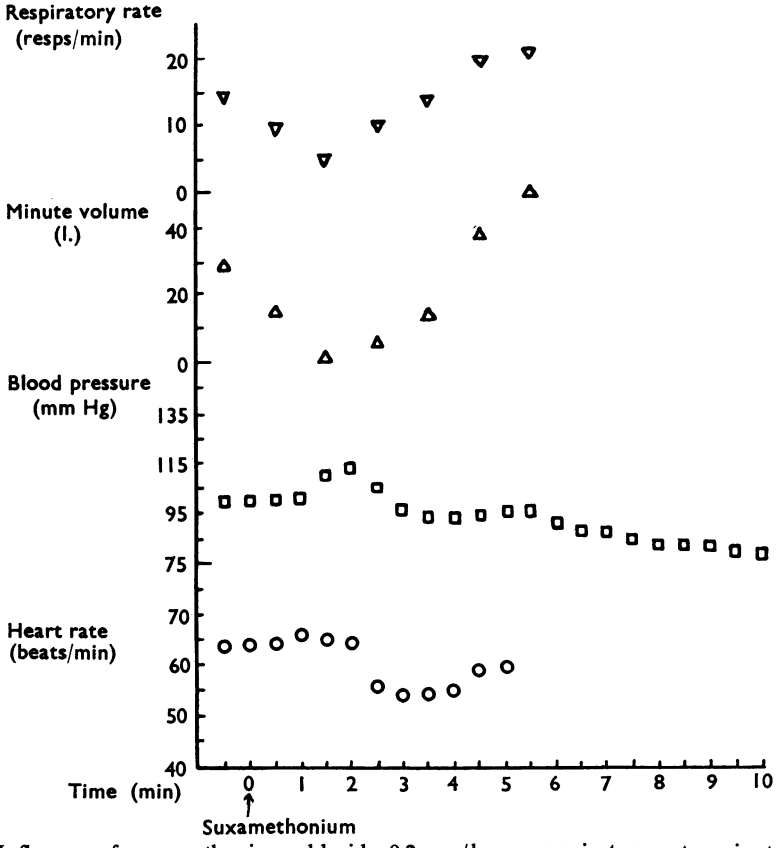

FIG. 9. Influence of suxamethonium chloride 0·2 mg/kg on respiratory rate, minute volume, blood pressure and heart rate of horses anaesthetized with di-ethyl ether. Each point represents the mean value for three experiments.

modified the cardiovascular actions of suxamethonium. In the present investigation the changes in cardiovascular and respiratory function produced by a clinical dose of the drug (0·146 mg/kg suxamethonium cation) in anaesthetized horses were monitored. At this dose level suxamethonium produced qualitatively similar changes in cardiovascular and respiratory function in more than twenty horses breathing spontaneously under halothane anaesthesia. The maximal increase in heart rate, occurring 1 to 1·5 min after injection of the drug, synchronized with the period of greatest reduction in minute volume, the maximal pressor response occurring on average 1 min later. In addition, it was found that the greatest rise in P_{CO_2} and the maximal reductions in P_{O_2} and pH values for arterial blood occurred in the samples taken at 2 and 3·5 min following the injection of suxamethonium. The changes in plasma electrolyte levels were typical of those normally associated with a respiratory acidosis, comprising increases in bicarbonate, potassium and sodium concentrations (Giebisch, Berger & Pitts, 1955 ; Siggaard-Anderson, 1962). The plasma potassium concentration, after returning almost to control levels, showed a secondary increase 12 min after administration of the drug. Stevenson (1960a, b), who also recorded a delayed rise in plasma potassium level following the administration of suxamethonium to dogs, attributed this response to release of potassium ion from voluntary muscle.

Further experiments demonstrated that the changes in cardiovascular function, following the administration of suxamethonium, were greatly reduced, but not abolished, when positive pressure ventilation was applied. It was therefore concluded that the principal effect of suxamethonium on the cardiovascular system could be ascribed to the depression of respiration, but it is also clear that suxamethonium can produce transient increases in heart rate and blood pressure by some other mechanism. It was shown that the ganglion blocking agent, hexamethonium bromide, completely antagonized the cardiovascular responses to suxamethonium. It is therefore likely, that those cardiovascular effects of suxamethonium that could not be attributed to respiratory depression, resulted from a stimulant action on peripheral autonomic ganglia, and possibly from an increased secretion of catecholamines from the adrenal medulla. Since positive pressure ventilation was not employed in these latter experiments further conclusions may be drawn. It is probable that the increases in heart rate and blood pressure, attributed to depressed respiratory function, were mediated reflexly via peripheral autonomic nerve fibres. This reflex component of the action of suxamethonium probably results from changes in blood pH and gas tensions and possibly from a temporary decrease in venous return to the heart. Some, or all, of these factors would presumably lead to increased activity in sympathetic vascoconstrictor nerves, together with an increase in sympathetic tone or decrease in vagal tone to the heart. A further effect of hexamethonium was an abolition of the muscular fasciculations, which normally preceded the changes in cardiovascular and respiratory function. The mode of action of hexamethonium in this respect is not clear but a similar effect has also been reported by Stevenson (1960b) in the dog.

Administration of propranolol, at a dose level of 0·1 mg/kg, partially antagonized the increase in heart rate and the pressor response to suxamethonium in six horses breathing spontaneously. This suggests that suxamethonium produces an increased sympathetic discharge to the heart. Moreover, in a single experiment it was found that the tachycardia produced by suxamethonium was abolished after the admini-

stration of propranolol at a dose level of 0·5 mg/kg. It would therefore appear that the increase in heart rate resulting from the respiratory depressant action of suxamethonium is mediated reflexly through an increased sympathetic tone to the heart, and not from a reduction in the resting vagal tone. To confirm this finding, however, it would be necessary to repeat this experiment in more animals.

The administration of four successive doses of suxamethonium led to a progressive reduction in the maximal increases in heart rate. In addition, the pressor response and the maximal reduction in minute volume were less pronounced with the second dose of suxamethonium but these parameters were not diminished further by the administration of the third and fourth doses of the drug. This development of tolerance is in contrast to the findings of Hansson (1958), who did not observe tachyphylaxis to suxamethonium in horses under pentobarbitone anaesthesia, and to the findings of Thesleff (1952) and Conway (1961) in the cat. Tachyphylaxis to the neuromuscular blocking and cardiovascular effects of suxamethonium has been recorded, however, by other workers in isolated muscle preparations (Freeman, 1967), and in the intact dog (Stevenson, 1960a), cat (Adams & Hall, 1962), and man (Graf *et al.*, 1963).

In all but one of the animals anaesthetized with halothane, the only observable effect of suxamethonium on the heart comprised a mild sinus tachycardia. In this horse the initial increase in heart rate was followed by a pronounced bradycardia. Since an unusually prolonged period of apnoea of 3·5 min duration occurred in this animal, this effect can probably be attributed to changes in blood pH, P_{O_2}, P_{CO_2} and electrolyte levels. Another atypical effect of suxamethonium on respiration was recorded in two other horses, which were in a deeper plane of anaesthesia than others in the series. Suxamethonium exerted its characteristic depressant effect on respiration, following which a large increase in tidal volume, and a pronounced reduction in respiratory rate occurred. This pattern of respiration lasted for approximately 25 min. Whether this unusual respiratory effect was due to some direct action of suxamethonium or to some other mechanism is not clear from the present results.

In a previous investigation in horses anaesthetized with pentobarbitone, Hansson (1958) attributed the cardiovascular responses to suxamethonium to the associated respiratory depression, because the responses were abolished when the animals were artificially ventilated. Adams & Hall (1962) and Stevenson & Hall (1959), on the other hand, ascribed the cardiovascular effects of suxamethonium to a nicotinic action on autonomic ganglia in horses under cyclopropane anaesthesia. From the present experiments it was concluded that stimulation of autonomic ganglia and respiratory depression both contributed towards the overall changes in cardiovascular function in horses anaesthetized with halothane. The differing findings of the present and previous authors may be due to the use of different general anaesthetic agents (Graf *et al.*, 1963). That the general anaesthetic may modify the cardiovascular effects of suxamethonium is apparent from the present results in horses anaesthetized with ether, in which only minor cardiovascular changes were recorded. The reason for the observed differences between ether and other anaesthetic agents in this respect has not been further investigated to date. It is nevertheless clear that the difference is not attributable to a shorter period of respiratory depression, because both the maximum reduction in minute volume and the duration of the period of respiratory depression were, on average, greater during ether than

during halothane anaesthesia. This finding is an agreement with the work of Katz (1966), who demonstrated that the neuromuscular blocking action of suxamethonium was potentiated by ether in the cat and, less consistently, in man.

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REFERENCES

ADAMS, A. K. & HALL, L. W. (1962). An experimental study of the action of suxamethonium on the circulatory system. *Br. J. Anaesth.*, **34**, 445–450.

BARRETO, R. S. (1960). Effect of intravenously administered succinylcholine upon cardiac rate and rhythm. *Anesthesiology*, **21**, 401–404.

BERETERVIDE, K. V. (1955). Actions of succinylcholine chloride on the circulation. *Br. J. Pharmac. Chemother.*, **10**, 265–269.

BOURNE, J. G., COLLIER, H. O. J. & SOMERS, G. F. (1952). Succinylcholine (succinoylcholine); muscle relaxant of short action. *Lancet*, **1**, 1225–1229.

BOVET, D., BOVET-NITTI, F., GUARINO, S., LONGO, V. G., FUSCO, R., & MAROTTA, M. (1949). Proprieta farmacodinaniche di aleuni derivati della succinilcolina dotati di azione curarica. *Rc. Ist sup. Sanita*, **12**, 106–137.

CONWAY, C. M. (1961). The cardiovascular action of suxamethonium in the cat. *Br. J. Anaesth.*, **33**, 560–564.

CRAYTHORNE, N. W. B., TURNDORF, H. & DRIPPS, R. D. (1960). Changes in pulse rate and rhythm associated with use of succinylcholine in anaesthetized children. *Anesthesiology*, **2**, 465–470.

DENTAN, M. & VOURC'H, G. (1967). Trouble du rhyhme cardiaque après injection intraveineuse de succinylcholine. *Anesth. Analg. Réanim.*, **24**, 529–534.

DOWDY, E. G. & FABIAN, L. W. (1963). Ventricular arrythmias induced by succinylcholine in digitalized patients: a preliminary report. *Anesth. Analg. curr. Res.*, **42**, 501–513.

FREEMAN, S. E. (1967). Ionic influences on succinylcholine blockade of the mammalian neuromuscular junction. *Br. J. Pharmac. Chemother.*, **32**, 546–566.

GALINO, A. H. & DAVIS, T. B. (1962). Succinylcholine and cardiac excitability. *Anesthesiology*, **23**, 32–40.

GEBISCH, G., BERGER, L. & PITTS, R. F. (1955). The extra renal response to acute acid-base disturbances of respiratory origin. *J. clin. Invest.*, **34**, 231–245.

GRAF, K., STRÖM, G. & WÅHLIN, A. (1963). Circulatory effects of succinylcholine in man. *Acta anaesth. scand.*, Suppl. XIV, 1–48.

HANSSON, C. H. (1958). Studies on the effect of succinylcholine in domestic animals. *Nord. vet. med.*, **10**, 201–216.

HOFMEYR, C. F. B. (1960). Some observations on the use of succinylcholine chloride (suxamethonium) in horses, with particular reference to the effect on the heart. *Jl S. Afr. vet. med. Ass.*, **31**, 251–259.

KATZ, R. L. (1966). Neuromuscular effects of diethyl ether and its interaction with succinylcholine and d-tubocurarine. *Anesthesiology*, **27**, 52–63.

LEIGH, M. D., MCCOY, D. D., BELTON, M. K. & LEWIS, G. B. (1957). Bradycardia following intravenous administration of succinylcholine chloride to infants and children. *Anesthesiology*, **18**, 698–702.

LUPPRIAN, K. G. & CHURCHILL-DAVIDSON, H. C. (1960). Effect of suxamethonium on cardiac rhythm. *Br. med. J.*, **2**, 1774–1777.

NEAL, P. A. & WRIGHT, J. G. (1959). The use of succinylcholine chloride as a casting agent in the horse prior to the induction of general anaesthesia. *Vet. Rec.*, **71**, 731–735.

PURPURA, D. P. & GRUNDFEST, H. G. (1956). Blockade of cardiac synapses by succinylcholine. *Science, N.Y.*, **124**, 319–320.

SIGGAARD-ANDERSON, O. (1962). Acute experimental acid-base disturbances in dogs. An investigation of the acid-base and electrolyte content of blood and urine. *Scand. J. clin. Lab. Invest.*, Suppl. 66.

SIGGAARD-ANDERSON, O. (1964). *The Acid-Base Status of the Blood.* Baltimore: Williams & Williams Co.

STEVENSON, D. E. (1960a). Changes in the blood electrolytes of anaesthetized dogs caused by suxamethonium. *Br. J. Pharmac. Chemother.*, **32**, 364–371.

STEVENSON, D. E. (1960b). A review of some side-effects of muscle relaxants in small animals. *J. small Anim. Pract.*, **1**, 77–83.

STEVENSON, D. E. & HALL, L. W. (1959). Pharmacological effects of suxamethonium. *Vet. Rec.*, **71**, 818.

TAVERNOR, W. D. (1959). The use of succincholine chloride as a casting agent in the horse. *Vet. Rec.*, **71**, 774.

TAVERNOR, W. D. (1960). The effect of succincholine chloride on the heart of the horse: clinical and pathological aspects. *Vet. Rec.*, **72**, 569–572.

TELFORD, J. & KEATS, A. S. (1957). Succinylcholine in cardiovascular surgery of infants and children. *Anesthesiology*, **18**, 841–848.

THESLEFF, S. (1952). Succinylcholine iodine. Studies on its pharmacological properties and clinical use. *Acta physiol. scand.*, **25**, Suppl. 99, 1–36.

WILLIAMS, C. H., DEUTSCH, S., LINDE, H. W., BULLOUGH, J. W. & DRIPPS, R. D. (1961). Effects of intravenous succinylcholine on cardiac rate, rhythm and blood pressure in anaesthetized man. *Anesthesiology*, **22**, 947–954.

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