THE MUSCLE RELAXANTS IN INFANTS AND CHILDREN*

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TWENTY YEARS have elapsed since Griffith's historic article¹ began a new era in anaesthesia. The story of modern anaesthesia is the story of the use of muscle relaxants.

Controversy has raged around the proper place of muscle relaxants in clinical anaesthesia. Some have tended to picture them as responsible for a high mortality.² Others have carefully examined the evidence and found their widespread use to be justified.³ Muscle relaxants have been particularly strongly condemned in infants and children as "exceedingly dangerous."⁴ The same author some years later has cautiously condoned their use.⁵

The findings and opinions in this paper are the result of some 6 years' experience at the Children's Hospital, Winnipeg, Manitoba. At its present capacity, about 4,500 general anaesthetics are given yearly to infants and children in this hospital, by a very small number of physician anaesthetists. Such concentrated experience has naturally led to the evolution of techniques, which cannot be recommended without reservations to those whose conditions of practice may be vastly different.

GENERAL INDICATIONS

Apart from their use in the diagnosis of myasthenic-like states and in the treatment of tetanus, as mentioned later, the chief uses of muscle relaxants are in general anaesthesia. Here they are employed to facilitate endotracheal intubation, for controlled respiration, and for better surgical operating conditions.

Almost all our patients having more than momentary anaesthesia are intubated. The benefits that muscle relaxants have conferred on adult surgery should not be denied to either the paediatric patient or the surgeon. The principles of light general anaesthesia with control of the airway, of respiration, and of muscle relaxation apply to infants and children, too.

CHOICE OF MUSCLE RELAXANTS

Only three muscle relaxants are presently used in our department. These are *d*-tubocurarine chloride, gallamine triethiodide, and succinylcholine. The third finds frequent use, especially in infants, while gallamine triethiodide is occasionally used for longer-acting muscle relaxation in larger children, and the venerable *d*-tubocurarine chloride is now used less and less.

This choice of muscle relaxants is determined by two factors: viz., the pattern of paediatric surgical practice and the sensitivity of infants. We are spared the

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demands of difficult upper abdominal surgery due to acquired disease, so common and so prolonged in adults. Intra-abdominal procedures in infants are done mostly for congenital anomalies. Nevertheless, our experience is contrary to the statements of others⁶ in that we have found muscle relaxants just as beneficial in these patients as in adults, and much appreciated by surgeons. It is true that the provision of continuous profound muscle relaxation, as sometimes required for a difficult cholecystectomy, is rarely, if ever, demanded in paediatric practice. But the stages of abdominal exploration and of peritoneal closure are greatly facilitated by the use of muscle relaxants, even in infants. Intrathoracic procedures are relatively more common in infants and children than in adults. The sensitivity of the infant to non-depolarizing drugs⁷ has made us avoid them.

ENDOTRACHEAL INTUBATION

This is employed for almost every anaesthetic given for more than a few minutes. It has been taught that intubation awake is easy and safer for the small infant. Somehow infants have been thought to become more rapidly hypoxic following the onset of apnoea than adults or larger children. No sound basis has been advanced for this opinion.

Succinylcholine, given intravenously in appropriate dosage, enables a completely atraumatic and unhurried intubation to be done even in infants, if the patient is first thoroughly oxygenated. It has been well demonstrated in adults⁸ and in dogs⁹ that apnoea following a brief period of thorough oxygenation may persist for several minutes before arterial oxygen desaturation becomes significant. Difficulty in obtaining arterial blood samples has discouraged similar work in infants during induction of anaesthesia. There has, however, been no clinical evidence of hypoxia. We have attempted to determine whether cerebral hypoxia does in fact occur by use of continuous electroencephalographic recordings. The results from two infants done under the customary clinical conditions are shown in Figure 1. No evidence of cerebral hypoxia is evident in the E.E.G. after 60 seconds of apnoea.

Attention to the details of this technique are important. We commonly induce anaesthesia in infants with cyclopropane and oxygen: for speed and flexibility this agent is unsurpassed. When the infant has stopped struggling (usually after three or four breaths of 40–50 per cent cyclopropane) anaesthesia is continued with halothane and oxygen. A flow rate of oxygen at least 2–3 times the infant's calculated minute volume and the use of an open-tailed bag prevent rebreathing of carbon dioxide and increasing concentrations of halothane from the bag. The infant is allowed to breathe this mixture of oxygen and about 2 per cent halothane quietly for at least three minutes. This is most important. Following the intravenous injection of succinylcholine and the onset of apnoea the face mask is removed and endotracheal intubation performed forthwith. It is not necessary to attempt to inflate the lungs with the bag before intubation; in fact in infants this may be difficult and can result in gastric dilatation with oxygen. We prefer to give succinylcholine intravenously than intramuscularly for endotracheal intubation, though the latter route may be safely used when necessary. Doses are described below.

FIGURE 1. Effect of 60 seconds apnoea on the well-oxygenated patient.

USE OF CONTROLLED RESPIRATION

Because of the small tracheal diameter endotracheal intubation enormously increases the resistance to spontaneous breathing in the infant.¹⁰ Controlled respiration is therefore advisable in all cases. For intrathoracic surgery it is essential both to ensure adequate ventilation and to facilitate the procedure. The use of intermittent intravenous doses of succinylcholine for this purpose is preferable, in our opinion, to hyperventilation. The latter may be quite unreliable in open-chest surgery.

In larger children controlled respiration is used only when a specific indication exists, as in intrathoracic surgery. In these patients, as in older children undergoing open-heart surgery, we use gallamine triethiodide for longer-acting muscle relaxation to ensure adequate ventilation with controlled respiration. Since we use halothane to control patient movement during the bypass, gallamine triethiodide has proved preferable to *d*-tubocurarine chloride. The total dose we have employed has not been more than 1 mg./lb. body weight and we have given our last dose well ahead of the time of bypass. In this way no residual curarization is present at the end of surgery.

DOSES OF SUCCINYLCHOLINE

Thesleff¹² made excellent observations on the action of this drug in man in 1952. He reported, among other things, that complete respiratory paralysis was not possible with doses of less than 0.4 mg./kg. body weight. The attitude of many anaesthetists to the dosage of succinylcholine is, unfortunately, blasé.¹¹ If asked, many scarcely know how much they have just used for endotracheal intubation. In adults the dose may vary between 40 and 100 mg. in different anaesthetists' hands. Thesleff recommended the use of an intravenous infusion of 0.1 per cent succinylcholine to give muscle relaxation. This has undoubtedly led to overdosage in many patients in the hands of those who regard strictly accurate dosage with this drug as unnecessary.

No ready explanation is available for the disappearance from the literature of reports of prolonged apnoea due to succinylcholine. The drug has not been discredited, its popularity is undiminished. The fault may often have been with the administrator. Overdosage has probably been common. Dual neuromuscular block due to doses of succinylcholine between 500 and 1,500 mg., but sometimes with doses as low as 100 mg., has been well described.¹³ Succinylmonocholine, a breakdown product of succinylcholine, may become an important cause of prolonged neuromuscular block at high dosage levels.¹⁴

In infants the use of an intravenous infusion of 0.1 or 0.2 per cent succinylcholine for muscle relaxation carries an inherent danger of circulatory overloading. That this technique carries also the danger of overdosage is obvious from the literature.¹⁵ Accurately controlled doses should be given intermittently as needed. The use of succinylcholine by intravenous drip has almost disappeared from our practice. Others are also having obvious doubts about overdosage in common clinical practice.¹⁶

We have attempted to arrive at a fairly accurate dose of succinylcholine for intubation based on the body weight of the patient. The results of this investigation are briefly presented.

MATERIAL

In this series 157 children were studied. Of these, 25 were under one year and 7 were new-born or under 30 days of age. The ages of the remainder ranged up to 14½ years.

Our usual induction techniques were followed, *i.e.*, cyclopropane, halothane, oxygen for new-born infants; rectal thiopental, cyclopropane, oxygen for larger children under 5–6 years of age; and intravenous thiopental for older children.

METHODS

Succinylcholine was given intravenously following the induction techniques just described. The drug was suitably diluted to allow accurate measurement of the dose given, usually five times in normal saline, but sometimes ten times for infants. The criterion of success was apnoea and complete laryngeal relaxation. A record was kept of each patient's age, height, weight, calculated surface area, the induction technique used, succinylcholine dose used, the duration of apnoea, and clinical relaxation. The drug dose used was based on body weight and a record was kept of drug/surface area ratio for each patient.

RESULTS

Table I shows how effective various doses were in our hands. With a dose of succinylcholine of 1 mg./4-5 lb. almost all children were easily intubated. The duration of apnoea ranged from 60 to 90 seconds and is somewhat shorter than one is accustomed to with larger doses. If this is considered to be a disadvantage, then it might be wiser to use a slightly larger dose.

TABLE I

Dosage	Number of patients	Number completely relaxed	Success
1 mg./16 lb.			
to 1 mg./6 lb.	30	15	50%
1 mg./4-5 lb.	125	119	95%
1 mg./3 lb.	2	2	100%

TABLE II

			Dosage
New-born to 1 month	7	6 successful 1 failed	1 mg./4-6 lb. 1 mg./7 lb.
1 month to 12 months	18	All successful	1 mg./4-5 lb.

Table II reveals, somewhat surprisingly, that infants are not markedly more resistant to succinylcholine than larger children. Apart from one failure with a dose of succinylcholine of 1 mg./7 lb., infants under 30 days were all well relaxed with doses ranging between 1 mg./4 lb. and 1 mg./6 lb. Infants between 1 and 12 months of age were all easily intubated with doses ranging between 1 mg./4 lb. and 1 mg./5 lb. We have never given succinylcholine to an awake infant but following a cyclopropane, halothane induction we have not been impressed by the infant's reputed resistance to this drug.⁷

The calculation of the drug/surface area ratio in infants and children is shown in Figure 2. With a dose of 1 mg./5 lb. body weight it is not surprising to find that in proportion to their surface area infants are receiving relatively less than larger children.

FIGURE 2. Dosage of succinylcholine 1 mg./5 lb. expressed in mg./sq. metre body surface area.

Intramuscular Dosage

We have found a dose of 1 mg./lb. body weight effective in infants in about 1 minute: intubation can be easily performed even if some respiratory movement is still present. Apnoea may persist for 10 minutes. Lack of predictability makes intramuscular very much inferior to intravenous use, in our opinion.

Use of Intermittent Dosage

This has almost completely replaced the use of 0.1 per cent or 0.2 per cent drip infusions in our practice, even in larger children. The requirements for control of respiration in infants having intrathoracic procedures are quite small. Difficulties in assessing the part played by hyperventilation and inhalation anaesthesia make dogmatic statements impossible. Examples of the doses used in two procedures, one intrathoracic and one intraabdominal, are given below.

TABLE III
DURATION OF ACTION
Intermittent succinylcholine: 1 mg./10 lb.
Female, age 2 months, weight 7 lb. 14 oz.
(Duration of action timed by stop-watch)

Succinylcholine (mg)	Duration of action
0 8	3'40''
0 8	4'02''
0 8	3'28''
0 8	3'25''
0 8	3'23''
0 8	3'26''
0 8	6'25''
0 8	3'08''
2 0	8'00''
3 2	7'30''
0 8	5'11''
12 4	51'38''

Table III shows the doses of succinylcholine used intermittently by the intravenous route during part of a pulmonary banding operation in a 2-month infant of weight 7 lb. 14 oz., with a ventricular septal defect and pulmonary hypertension. The duration of apnoea was timed by stop-watch, the diaphragm being observed directly. Continuous E.E.G. and E.K.G. recordings showed an uneventful course of light anaesthesia. Body temperature was maintained normal throughout by a water mattress. The two relatively large doses shown were given during a delicate part of the procedure when pressure recordings were being made, anaesthesia was extremely light, and any movement would have been exceedingly dangerous.

Table IV shows the doses of succinylcholine used intravenously during part of an intra-abdominal operation. This 11-day-old infant, weighing 6 lb. 2 oz., had surgery performed for relief of intestinal obstruction. Once more the small doses required are noteworthy. Total doses of the order of 11-12 mg. per hour in infants are a far cry from those described in the literature¹⁵ and yet in both the cases described respiratory control was very easy and, in the second, abdominal

TABLE IV
DURATION OF ACTION
Intermittent succinylcholine: 1 mg./8 lb.
Male, age 11 days, weight 6 lb. 2 oz.

Anaesthesia	Succinylcholine (mg.)	Duration of action (min.)	Operation
Nitrous oxide, oxygen, halothane 0.5%	0 8	4	Incision to peritoneum
	0 8	4	
	0 8	4	
	0 8	5	
Nitrous oxide, oxygen	0 8	4	Intra-abdominal
	0 8	4	
	0 8	4 5	
	0 8	4 5	
Nitrous oxide, oxygen	0 4	3	Closing
	0 8	3 5	
	0 8	3 5	
	0 8	4	
0.5% halothane	0 8	4	
Totals	10 0	52	

relaxation was provided at will. Neither the supposed resistance of the newborn to succinylcholine nor the theoretical possibility that intermittent doses might lead to overdosage¹⁷ is supported by our findings, of which these are typical examples.

Effects of Muscle Relaxants on the Cardiovascular System

The hypotensive effects of large doses of *d*-tubocurarine chloride when given rapidly intravenously are well known. The exaggeration of this effect, which occurs when halothane is used, has made us avoid *d*-tubocurarine chloride for open-heart surgery. Two cases of complete heart block that have occurred in our experience when this combination was used during surgery for closure of atrial septal defects have further discouraged us. Nevertheless others have satisfactorily used *d*-tubocurarine chloride for open-heart surgery.⁵

Gallamine triethiodide in clinical doses causes marked tachycardia in children within 30–45 seconds of its intravenous injection. This cardiac vagolytic action has been found useful to protect the heart against reflex vagal stimulation as investigated and reported by us in patients undergoing strabismus surgery.¹⁸

The cardiovascular effects of intravenous succinylcholine are at present the centre of many investigations, and are likely to prove much more complex than we have suspected. Much confusion exists at present. Although tachycardia has been found by some to be the predominant effect,¹⁹ most workers have noted significant bradycardia.^{20,21} This has been described as typically occurring after second or third injections,²¹ although in our experience it can occur following the initial injection of succinylcholine. However, it is more common to find that the initial injection causes tachycardia, while subsequent injections result in bradycardia due to various degrees of heart block or nodal rhythm (Fig. 3).

Recent interesting experimental work has suggested that arrhythmias may be due to a direct myocardial action as well as a post-ganglionic sympathetic stimulation.²² This work has suggested that the time during which the heart is exposed

FIGURE 3

to the drug may be important as well as the dose. However, in their experiments in monkeys, whose response to succinylcholine is supposed to be similar to that of humans, doses of the order of 2 mg./kg. body weight were given every six minutes for an hour. In a 70 kg. adult this would mean 1,400 mg. in an hour, so here we are once more considering clinical overdosage.

The bradycardia that occurs following intravenous succinylcholine injection during anaesthesia is said to be preventable by intravenous atropine injection. That the dose of atropine required may be heavy is suggested by Table V, in which bradycardia occurred in spite of 0.4 mg. atropine given 50 minutes pre-operatively and an additional 0.4 mg. given intravenously 5 minutes before injection of succinylcholine.

Contraindications

In general, muscle relaxants are avoided in children in the presence of upper respiratory obstruction and when technical problems are expected to be great during intubation.

TABLE V
FAILURE TO PREVENT SUCCINYLCHOLINE BRADYCARDIA
WITH INTRAVENOUS ATROPINE

Female, age 14 years, weight 140 lb.
Atropine 0.4 mg. 50 minutes preoperatively
Atropine 0.4 mg. intravenously 5 minutes
before first injection of succinylcholine

Time after 0.4 mg I.V. atropine (min.)	I.V. Succinyl- choline (mg.)	Pulse	Time (sec.)
5	20	120	0
		66	15
		90	25
		120	60
9	20	120	0
		84	15
		96	25
		120	60
13	20	120	0
		84	15
		100	25
		114	60

Certain special circumstances make the use of these drugs unwise. Succinylcholine given intravenously usually causes a rise in intraocular pressure.^{23,24} It appears that the extraocular muscles behave differently from other muscles in developing a prolonged contraction in response to succinylcholine, though this has not been conclusively proved. In operations for congenital glaucoma, for cataracts and penetrating eye injuries, we avoid the use of succinylcholine.

Succinylcholine is best avoided for relaxation in closure of the peritoneum of infants with congenital diaphragmatic hernia, for mechanical reasons.⁵

General body hypothermia certainly appears to prolong the duration of action of depolarizing muscle relaxants.^{25,26} When we are deliberately employing hypothermia we avoid the use of this drug except for endotracheal intubation; and in cases when succinylcholine is being employed intermittently over a long period of time it is important to prevent body cooling by placing the infant or child on a water mattress kept at normal body temperature.

Non-depolarizing muscle relaxants are contraindicated in infants and in patients with myasthenic-like states. We also avoid them in children with diminished pulmonary function as in patients with residual poliomyelitis undergoing surgery for spinal fusion.

Deaths due to cardiac arrest in children with chronic burns have been attributed to succinylcholine. A recent article reviewing this subject points out that all these cases have certain startling similarities.²⁷ Succinylcholine may have some deleterious effects on the heart in these special cases.²⁸ The drug can be used with safety in serious and extensive burns in the early stages, but in these late burns, after the third week, it is probably better avoided till the situation has been further investigated.

Trends in the Use of Muscle Relaxants

In anaesthesia at the Children's Hospital, Winnipeg, the tendency is to use

non-depolarizing relaxants very infrequently indeed, except for teaching their use to residents.

Succinylcholine is being used in doses that are certainly smaller and more accurately administered than formerly, and almost entirely by intermittent intravenous injection. The introduction of halothane has somewhat reduced the frequency of use of succinylcholine both for endotracheal intubation and for controlled respiration. With halothane, both of these ends can be rapidly and easily attained and it is important in the training of residents that more than one technique be acquired where possible. This opinion is held in other teaching centres also.²⁹

Diagnostic and Therapeutic Uses

The use of *d*-tubocurarine chloride or gallamine triethiodide in the diagnosis of myasthenia gravis is well known. We have used one-tenth the intubating dose of gallamine triethiodide, *i.e.*, about 1 mg./10 lb., as a diagnostic test. Sensitivity to curare is not diagnostic of myasthenia gravis exclusively. The brother and sister whose photographs are shown (Fig. 4) had markedly positive curare tests

FIGURE 4

but were not myasthenics. Their case histories are reported in detail elsewhere.³⁰ Patients with carcinomatous neuropathy are also reported to show abnormal responses to muscle relaxants.³¹

The use of muscle relaxants in the treatment of tetanus is no longer widely proclaimed. A moderately severe case was treated by us in 1956 with barbiturates, zoxazolamine, and myanesin with good results.³² Success with drugs acting on the reticular activating substance has made it possible to manage such patients without paralysis of respiration and the heavy responsibilities of such drastic measures.³³

SUMMARY

Many anaesthetists have been reluctant to apply the use of muscle relaxants to anaesthesia for infants and children. Endotracheal intubation, controlled respiration, and muscle relaxation are facilitated by the use of these drugs to the advantage of both patient and surgeon, in infants and children as much as in adults.

Succinylcholine is used a great deal in anaesthesia at the Children's Hospital, Winnipeg. If a technique of careful oxygenation is carried out, it has been shown to be quite safe for unhurried intubation even in the new-born. Investigation has revealed that the effective dose for both intubation and control of respiration is far less than is commonly taught and that the new-born is not as markedly resistant to succinylcholine as many have said. The use of intravenous infusions of 0.1 per cent and 0.2 per cent succinylcholine is a common cause of overdose and is seldom employed at this hospital even for large children.

The effects of succinylcholine on the cardiovascular system are complicated. The bradycardia that occurs may require large intravenous doses of atropine to abolish it. These arrhythmias are apparently not dangerous in most cases. In chronic burns, however, the drug has a sinister reputation and is best avoided at the present time.

Gallamine triethiodide is the drug commonly employed for longer-acting muscle relaxation. Tachycardia caused by this drug may be useful in strabismus surgery.

Obstruction of the airway, congenital glaucoma, surgery for cataracts and penetrating eye injuries contraindicate succinylcholine, while hypothermia prolongs its action. Infancy, myasthenic-like states, and diminished respiratory function contraindicate curare-like drugs.

The use of the curare sensitivity test to diagnose myasthenic-like states and the diminishing importance of relaxants in treating tetanus are mentioned.

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RÉSUMÉ

De nombreux anesthésistes se servent de médicaments myorésolutifs avec réluctance dans l'anesthésie des nouveaux-nés et des enfants. Les médicaments

myorésolutifs aident les adultes énormément, et ils peuvent être tout aussi utiles pour l'intubation endotrachéale, la respiration contrôlée et la relaxation des muscles dans l'anesthésie des nouveaux-nés et des enfants, à l'avantage du malade et du chirurgien.

On se sert beaucoup du chlorure du succinylcholine à l'Hôpital Des Enfants de Winnipeg. Si on emploie une technique prudente d'oxygénation, il a été démontré qu'une intubation sans hâte est sans danger même chez le nouveau-né. Après investigation, il a été révélé que la dose efficace pour l'intubation et le contrôle de la respiration est beaucoup moindre que l'on pense, et le nouveau-né n'est pas aussi remarquablement résistant au chlorure du succinylcholine que beaucoup l'ont dit. L'usage d'infusions intraveineuses de 0.1 et 0.2 pour cent au chlorure du succinylcholine est une cause commune de dose exagérée, et très peu employé à cet hôpital même pour les enfants plus grands.

Les effets du chlorure du succinylcholine sur le système circulatoire sont très compliqués. Dans certains cas, il peut être nécessaire d'administrer d'importantes doses d'atropine par voie intraveineuse pour contrôler la bradycardie. Ces irrégularités particulières du coeur ne sont pas dangereuses apparemment dans la plupart des cas. Mais dans le cas de brûlures chroniques, le médicament a une réputation sinistre, et il est mieux de l'éviter à ce moment-là.

Le triodure de gallamine est le médicament communément employé pour une relaxation plus prolongée des muscles. La tachycardie qui en résulte peut être utile dans la chirurgie extraoculaire.

L'obstruction du passage respiratoire, le glaucome congénital, la chirurgie pour les cataractes et blessures pénétrantes de l'oeil, contre-indiquent le chlorure du succinylcholine, et l'hypothermie prolonge son action. Les maladies qui ressemblent à la myasthénie, et les conditions dans lesquelles la fonction respiratoire est diminuée, contre-indiquent les médicaments comme le chlorure de *d*-tubocurare.

Cet article fait mention de l'usage du triodure de gallamine dans le diagnostic de la myasthénie, et du fait que les médicaments myorésolutifs deviennent moins importants dans la thérapie du tetanos.

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