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The Response of Denervated Skeletal Muscle to Succinylcholine

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The responses of denervated and normal canine gastrocnemius muscle to succinylcholine (SCh) were compared and contrasted in regard to potassium (K^+) flux $\dot{V}_{O_2}$, muscle tension, and electrical activity. K^+ efflux and $\dot{V}_{O_2}$ of denervated muscle increased 20-fold and fourfold after SCh, respectively, while K^+ efflux and $\dot{V}_{O_2}$ of normal muscle did not change and initially doubled, respectively. Denervated muscle responded to SCh with a contracture, as manifested by a prolonged increase in muscle tension and by prolonged electrical silence and inexcitability. Prior treatment with gallamine in paralyzing doses prevented increases in K^+ flux and $\dot{V}_{O_2}$; small doses of gallamine attenuated these increases but did not block them. These effects are probably related to an increase in sensitivity of the muscle membrane that develops following denervation such that SCh produces a mass depolarization of the muscle, diffusely increasing membrane permeability to Na^+ and K^+, and thereby stimulating the Na^+/K^+ pump. (Key words: Contracture; Denervation; Hyperkalemia; Skeletal Muscle; Succinylcholine.)

HYPERKALEMIA following intravenous administration of succinylcholine (SCh) has been demonstrated in patients with extensive burns,[1] massive trauma,[2] and neuromuscular disorders involving loss of motor function with resultant atrophy.[3] All evidence indicates that in each of these situations the hyperkalemia results from release of unusual amounts of potassium (K^+) from abnormal skeletal muscle,[4, 5] but previous reports have provided only qualitative information.[2, 6, 7] The present study provides quantitative information about the release of K^+ from denervated dog gastrocnemius muscle, demonstrates a concomitant increase in oxygen consumption ($\dot{V}_{O_2}$) in muscle, and compares the blocking effects of partially and totally paralyzing doses of gallamine.

Material and Methods

Unilateral sciatic nerve section, right or left, was performed at the inferior margin of the gluteus maximus muscle in 20 mongrel dogs (weights, 17 to 33 kg) during anesthesia with pentobarbital sodium (25 mg/kg, intravenously). Postoperatively, the dogs were cared for in individual pens by experienced handlers. Then, 24 to 42 days later, the dogs were anesthetized with thiopental sodium (15 to 20 mg/kg, intravenously), the tracheas were intubated, and the lungs were ventilated by a Harvard pump with a mixture of halothane, O_2, and N_2. Ventilation and gas concentrations were adjusted to maintain Pa_{CO_2} at 38 to 42 torr, Pa_{O_2} at 100 to 120 torr, and mean expired halothane concentration at 1.0 ± 0.2 per cent (infrared analyzer). Catheters were placed in a carotid artery for sampling and pressure measurements (strain gauge) and in two peripheral veins for infusion of fluids and drugs and for return of externally collected blood. The venous drainages of both the normal and denervated gastrocnemius muscles were isolated and collected with suitable precautions.[8] Muscle and body temperatures were maintained at 37.0 ± 0.2 C.

Net fluxes of muscle K^+ and muscle $\dot{V}_{O_2}$ were calculated by means of the Fick formula, from direct measurements of muscle blood flow and the differences between muscle venous and arterial whole-blood K^+ and O_2 contents. For example:

$$K^+ \text{ efflux} = MBF \times (K^+_{M_v} - K^+_a)$$

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where MBF represents muscle blood flow; K^+_{Mv}, K^+ in muscle venous whole blood; K^+_a, K^+ in arterial whole blood. A negative value indicates influx. K^+ flux and $\dot{V}_{O_2}$ were calculated from average values of multiple determinations of each entity for each 10-minute period of observation. Serum K^+ and whole-blood K^+ were determined by a flame photometer (Instrumentation Lab, Lexington, Mass.). Blood O_2 content was calculated from determinations of P_{O_2} and HbO_2, as previously described.[8] When all observations had been completed, both muscles were removed, weighed, and biopsied, and the tissue samples were assayed for K^+.[9]

The response to a single intravenous injection of SCh (0.25 mg/kg) was determined for the following circumstances: without prior drugs (five dogs); with total paralysis initiated 30 minutes previously and maintained by continuous infusion of gallamine (3 mg/kg initially and 4 mg/kg/hour, five dogs); after ouabain (0.05 or 0.1 mg/kg given one hour before, one dog being used for the study of each dose). Control observations in each case were made in triplicate simultaneously for both normal and denervated muscle. SCh then was given, and the measurements were repeated ten times during the next hour. Significance of differences was tested between and within groups using the unpaired or paired t test, $P < 0.05$ being considered significant.

The same basic protocol was followed for the study of a smaller (0.025 mg/kg) and a larger (2.5 mg/kg) dose of SCh without prior drugs, one dog being used for the study of each dose. Additionally, the response to the original dose of SCh (0.25 mg/kg) was determined when the administration of SCh was preceded (5 minutes) by a partially paralyzing dose of gallamine (0.5 mg/kg; five dogs). Control observations in this group were made immediately before injection of gallamine.

In one additional dog, the preparation was used exclusively to observe (oscillographic display) denervated muscle action potentials (concentric needle electrode) and denervated muscle tension changes (strain gauge, 100 g tension initially) after SCh (0.25 mg/kg).

Results

Effect of Gallamine

In the absence of gallamine, SCh produced a massive efflux of K^+ from denervated muscle (fig. 1, table 1). This response was prevented by the prior injection of paralyzing doses of gallamine. The $\dot{V}_{O_2}$ of denervated muscle increased fourfold with SCh, and this increase also was blocked by the prior injection of paralyzing doses of gallamine (fig. 2, table 1). These increases in K^+ efflux and $\dot{V}_{O_2}$ were maximal 1 to 3 minutes after SCh administration and they then steadily lessened, in a pattern similar to that for plasma K^+ (fig. 3, table 2). Muscle blood flow initially increased threefold and remained above control values for 30 minutes (table 1).

For normal muscle, control K^+ efflux and $\dot{V}_{O_2}$ were similar to and less than control K^+ efflux and $\dot{V}_{O_2}$ of denervated muscle, respectively (table 1). Neither control relationship was altered by prior administration of gallamine. After SCh alone, K^+ efflux did not change and $\dot{V}_{O_2}$ increased; after the combination of gallamine and SCh, neither K^+ efflux nor $\dot{V}_{O_2}$ changed (table 1).

Effects of Different Doses of Succinylcholine

K^+ effluxes of denervated muscle with three doses of SCh—0.025 mg/kg, 0.25 mg/kg, and 2.5 mg/kg—are illustrated in figure 4. In denervated muscle, K^+ effluxes of about equal magnitude were noted after the two larger doses of SCh. In normal muscle, no change of K^+ efflux was evident at these doses, but fasciculations and relaxation of normal muscle were observed. The smallest dose of SCh produced neither a change of K^+ efflux nor fasciculations and relaxation of normal muscle. Yet in denervated muscle the smallest dose produced an increase in K^+ efflux that was nearly half that produced by the higher doses of SCh. These findings indicate supersensitivity in the denervated muscle. The $\dot{V}_{O_2}$ of denervated muscle responded to the three doses in a manner parallel to the changes in K^+ efflux (not tabulated).

Increases in K^+ efflux were followed by K^+ influx in all situations (figs. 1 and 4), but during the 60 minutes of observation, K^+ influx never completely balanced the prior efflux.

TABLE 1. K^+ Efflux, $\dot{V}_{O_2}$s, and Blood Flows of Denervated and Normal Muscle after SCh (0.25 mg/kg, Five Dogs Each, Mean ± SE)

	Gallamine	Muscle	Control	Minutes after SCh					
				0-10	10-20	20-30	30-40	40-50	50-60
K^+ efflux, μEq/min/100 g	None	Normal	2.9 ± 1.7	1.7 ± 1.0	0.7 ± 0.2	0.7 ± 0.5	0.5 ± 0.3	0.4 ± 0.3	0.0 ± 0.3
		Denervated	4.5 ± 2.2	91.4* ± 8.0	23.3* ± 8.1	3.0 ± 0.9	0.0 ± 5.4	−2.3 ± 4.2	−3.3 ± 2.0
	4 mg/kg/hour	Normal	1.7 ± 0.3	1.8 ± 0.6	1.4 ± 0.5	1.2 ± 0.6	0.9 ± 0.6	0.6 ± 0.5	0.8 ± 0.5
		Denervated	2.9 ± 1.4	3.9 ± 0.8	1.9 ± 0.5	0.9 ± 0.5	0.3 ± 0.5	0.5 ± 0.3	0.8 ± 0.3
$\dot{V}_{O_2}$, ml/min/100 g	None	Normal	0.83 ± 0.12	1.53* ± 0.24	1.28* ± 0.27	1.08 ± 0.19	0.87 ± 0.10	0.85 ± 0.16	0.82 ± 0.11
		Denervated	1.21 ± 0.23	4.77* ± 0.74	3.00* ± 0.87	2.07* ± 0.79	1.04* ± 0.45	1.72* + 0.33	1.01* ± 0.24
	4 mg/kg/hour	Normal	0.81 ± 0.18	0.77 ± 0.16	0.74 ± 0.15	0.73 ± 0.14	0.81 ± 0.13	0.78 ± 0.13	0.74 ± 0.10
		Denervated	1.39 ± 0.15	1.30 ± 0.13	1.34 ± 0.12	1.32 ± 0.13	1.33 ± 0.13	1.39 ± 0.16	1.18 ± 0.10
Muscle blood flow, ml/min/100 g	None	Normal	15.0 ± 3.5	19.2 ± 3.5	13.8 ± 2.9	11.5 ± 2.0	10.1 ± 1.6	9.8 ± 1.6	8.9* ± 1.5
		Denervated	19.4 ± 6.0	56.3* ± 9.8	48.7* ± 8.3	41.0* ± 7.3	33.2 ± 5.4	26.0 ± 4.0	20.6 ± 2.7
	4 mg/kg/hour	Normal	10.6 ± 1.3	8.7 ± 1.5	7.6* ± 1.1	7.8* ± 0.8	7.9* ± 0.7	8.1* ± 0.7	7.6* ± 0.8
		Denervated	17.6 ± 1.5	14.7 ± 1.1	13.5* ± 1.0	13.4* ± 0.9	13.5* ± 0.9	13.7* ± 0.9	13.3* ± 1.1

* Significantly different from control, $P < 0.05$, t test for paired data.

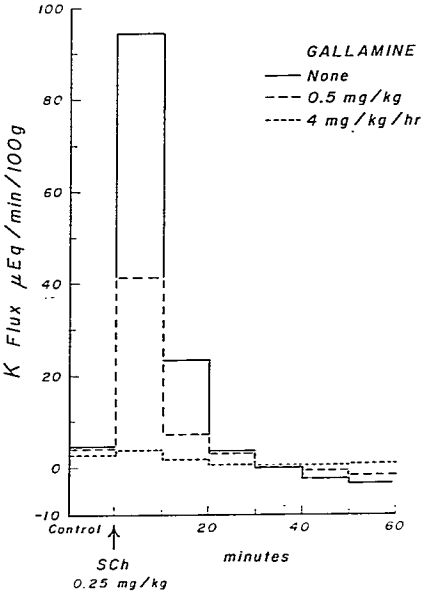

FIG. 1. K^+ flux of denervated muscle after SCh injection and modification by prior administration of gallamine. Efflux is indicated by positive values, influx by negative values.

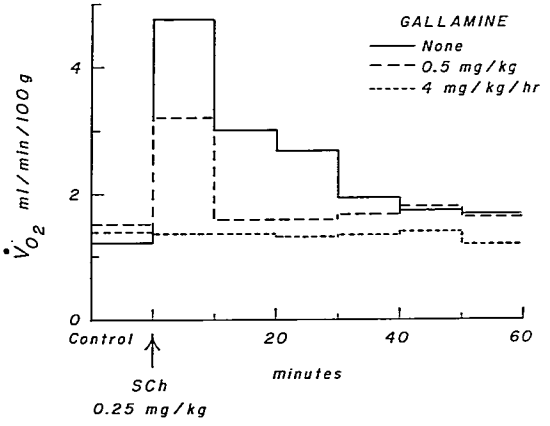

FIG. 2. $\dot{V}_{O_2}$ of denervated muscle after SCh injection and modification by prior administration of gallamine.

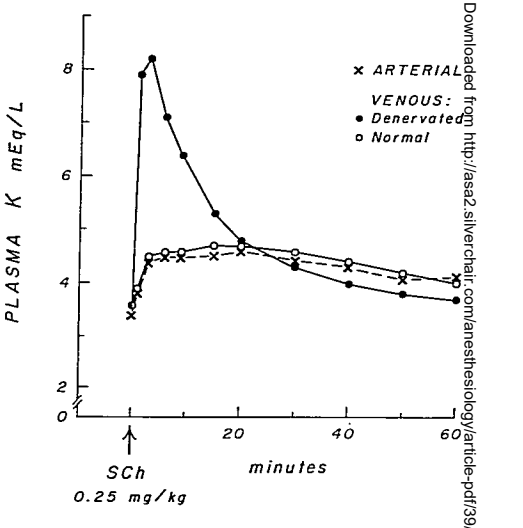

FIG. 3. Changes in plasma K^+ concentrations of arterial and muscle venous blood (denervated and normal) following injection of SCh (0.25 mg/kg). (0 time values are means of control observations.)

Prior administration of ouabain—either 0.05 or 0.1 mg/kg—did not alter the response to SCh of either K^+ flux or $\dot{V}_{O_2}$.

ELECTROMYOGRAPHY

The control electromyogram of denervated muscle showed frequent spontaneous action potentials (fibrillation potentials [10]), which became more frequent with needle movement (insertion activity, fig. 5). After injection of SCh (fig. 5), there was a 15-second explosive burst of action potentials, followed by a 30-minute period of electrical silence, during which the muscle was not excitable by needle movement. Spontaneous activity and excitability to needle movement then slowly returned, but at 60 minutes were still diminished. Denervated muscle tension after injection of SCh increased rapidly to a tension exceeding 225 g (off scale) and slowly decreased, but at 60 min it still amounted to 155 g. Fasciculations were not observed in the denervated muscle after SCh injection.

Denervated muscle weighed less than normal muscle (table 3). In the absence of prior K^+ efflux, the K^+ content of denervated muscle was lower than that of normal muscle (table 3, line 2). After SCh-induced efflux with minimal influx (fig. 1, gallamine = "none"), the K^+ content of denervated muscle tended to decrease further, but not quite enough to be significant (table 3, line 1, D/N ratio).

Changes in mean arterial pressure and arterial P_{O_2}, P_{CO_2}, *pH*, and buffer base were insignificant in all groups (not tabulated).

Discussion

The response of denervated gastrocnemius muscle to SCh clearly differed from that of normal muscle: efflux of K^+ from denervated muscle increased 20-fold, while efflux from normal muscle did not change; the $\dot{V}_{O_2}$ of denervated muscle increased fourfold, while the $\dot{V}_{O_2}$ of normal muscle only doubled; denervated muscle developed a persistent contracture, while normal muscle fasciculated and relaxed. We believe that these findings reflect the change in receptor properties of the membrane of denervated muscle.

The receptor area of denervated muscle is known to enlarge progressively until virtually the entire surface membrane of the muscle

TABLE 2. K^+ Concentrations (mEq/liter) in Arterial, Denervated Muscle Venous, SCh (0.25 mg/kg)

Gallamine	Source of Sample	K^+ Concentration			
		Control	1	3	6
Plasma					
None	Arterial	3.4 ± 0.2	3.8 ± 0.1	4.4* ± 0.2	4.5* ± 0.2
	Denervated muscle venous	3.6 ± 0.2	7.9* ± 0.4	8.2* ± 0.5	7.1* ± 0.4
	Normal muscle venous	3.6 ± 0.2	3.9* ± 0.1	4.5* ± 0.1	4.6* ± 0.1
4 mg/kg/hour	Arterial	3.5 ± 0.1	3.5 ± 0.1	3.6 ± 0.1	3.6 ± 0.1
	Denervated muscle venous	3.9 ± 0.1	4.0 ± 0.1	4.2* ± 0.1	4.2* ± 0.1
	Normal muscle venous	3.8 ± 0.1	3.9 ± 0.1	4.0* ± 0.1	4.0* ± 0.1
Whole blood					
None	Arterial	4.8 ± 0.2	5.3 ± 0.4	5.6* ± 0.4	5.6* ± 0.4
	Denervated muscle venous	5.1 ± 0.3	7.8* ± 0.3	7.7* ± 0.3	7.2* ± 0.3
	Normal muscle venous	5.1 ± 0.3	5.4 ± 0.3	5.7* ± 0.3	5.8* ± 0.3
4 mg/kg/hour	Arterial	4.7 ± 0.2	4.6 ± 0.1	4.7 ± 0.1	4.7 ± 0.1
	Denervated muscle venous	4.8 ± 0.1	4.9 ± 0.1	5.0 ± 0.1	5.0 ± 0.2
	Normal muscle venous	4.8 ± 0.1	4.8 ± 0.1	4.8 ± 0.1	4.9 ± 0.2

* Significantly different from control; $P < 0.05$, t test for paired data.

fiber develops the greater sensitivity to chemical depolarization that is peculiar to endplates.[5] SCh, acting as does acetylcholine on denervated muscle,[10] then depolarizes the entire (supersensitive) membrane at one time, and produces a burst of action potentials followed by a contracture. By definition, a contracture is a nonpropagated prolonged reversible activation of the contractile mechanism, usually associated with sustained depolarization.[11] The large area of supersensitive membrane continuously loses intracellular K^+ as long as it is depolarized [12]; the extracellular concentration of K^+ thus is increased and some of this is lost to the venous circulation. The increased extracellular K^+ stimulates the Na^+/K^+ pump,[13] and thus increases the $\dot{V}_{O_2}$, which is additionally increased because of the contracture. The increase in muscle blood flow may be due to a mechanism similar to that reported for vasodilation in exercising skeletal muscle, namely, release of ATP from the contracting muscle.[14]

The long duration of the response to SCh in denervated muscle is probably related to supersensitivity. The usual paralyzing dose of SCh in normal muscle is excessive for the supersensitive membrane of denervated muscle. The supersensitive membrane also may be unusually responsive to metabolites of SCh. Furthermore, both SCh and its metabolites may be bound by receptor sites in the membrane.[1]

The supersensitivity phenomenon may be modified in several ways. The effect of gallamine is consistent with the assumption that depending on dose, it occupies some or all of the receptor sites, thus limiting or preventing the action of SCh. A similar effect has been reported to occur with curare.[15, 16] Other agents that modify the phenomenon include those antibiotics that may prevent the protein synthesis necessary for development of extrajunctional receptors,[17] those antibiotics that may greatly stimulate the Na^+/K^+ pump [18] (thus increasing its effectiveness), and intermittent electrical stimulation following denervation, which may prevent atrophy and supersensitivity.[19]

Ouabain, which inhibits the Na^+/K^+ pump, should block that part of the increase in $\dot{V}_{O_2}$ caused by stimulation of the pump, and it should also prolong the efflux of K^+. Yet doses of 0.05 mg/kg and 0.1 mg/kg neither affected the magnitude or duration of the increase in $\dot{V}_{O_2}$ nor prolonged the efflux of K^+—even though a dose of 0.1 mg/kg is 80 per cent of the canine fatal dose.[20] While increased extracellular K^+ opposes this inhibition, data from

and Normal Muscle Venous Plasma and Whole Blood in Relation to Gallamine and Five Dogs Each, Mean ± SE)

(mEq/l) at Various Times (Minutes) after SCh Injection

9	15	20	30	40	50	60
4.5* ± 0.2	4.5* ± 0.2	4.6* ± 0.1	4.4* ± 0.1	4.3* ± 0.2	4.1* ± 0.2	4.1* ± 0.2
6.4* ± 0.2	5.3* ± 0.2	4.8* ± 0.2	4.3* ± 0.2	4.0 ± 0.2	3.8 ± 0.2	3.7 ± 0.2
4.6* ± 0.1	4.7* ± 0.1	4.7* ± 0.1	4.6* ± 0.1	4.4* ± 0.1	4.2* ± 0.2	4.0 ± 0.2
3.6 ± 0.1	3.8* ± 0.1	3.8* ± 0.1	3.8* ± 0.1	3.8* ± 0.1	3.7 ± 0.2	3.8* ± 0.1
4.1* ± 0.1	4.1* ± 0.1	4.0 ± 0.1	4.0 ± 0.1	3.9 ± 0.1	3.9 ± 0.1	4.0 ± 0.1
4.1* ± 0.1	4.1* ± 0.1	4.2* ± 0.1	4.1* ± 0.1	4.1* ± 0.1	4.0* ± 0.1	4.0* ± 0.1
5.7* ± 0.3	5.4* ± 0.2	5.7* ± 0.3	5.7* ± 0.3	5.6* ± 0.3	5.5* ± 0.3	5.4* ± 0.3
6.7* ± 0.3	5.8* ± 0.2	5.8* ± 0.3	5.7* ± 0.4	5.5 ± 0.3	5.3 ± 0.3	5.2 ± 0.3
5.8* ± 0.3	5.5* ± 0.1	5.8* ± 0.3	5.8* ± 0.3	5.6* ± 0.3	5.5* ± 0.3	5.3 ± 0.3
4.7 ± 0.1	4.8 ± 0.1	4.8 ± 0.2	4.9 ± 0.1	5.0* ± 0.1	5.0* ± 0.1	5.1* ± 0.1
4.9 ± 0.1	4.9 ± 0.2	4.9 ± 0.1	5.0 ± 0.1	5.0 ± 0.1	5.1* ± 0.1	5.1* ± 0.1
4.9 ± 0.1	5.0 ± 0.2	5.0 ± 0.2	5.0 ± 0.2	5.1* ± 0.1	5.1* ± 0.1	5.2* ± 0.1

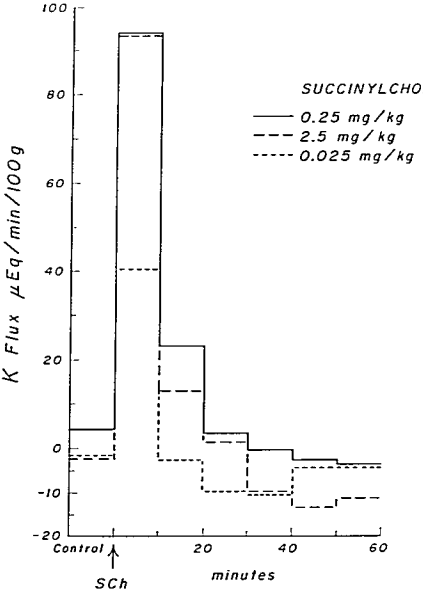

FIG. 4. K^+ flux of denervated muscle after injection of SCh (0.025 mg/kg, one dog; 0.25 mg/kg, mean, five dogs; 2.5 mg/kg, one dog). Efflux indicated by positive values, influx by negative values.

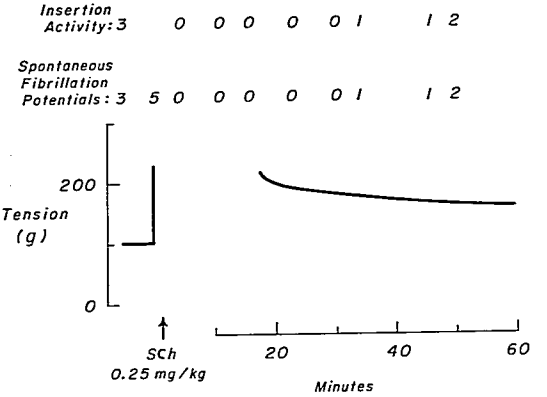

FIG. 5. Electrical activity (concentric needle electrode) and tension of denervated muscle after injection of SCh (0.25 mg/kg, one dog). (See text for details.)

only two animals are insufficient to enable one to speculate on the significance of the lack of effect of ouabain.

Although the K^+ content of denervated muscle was less than that of normal muscle, the concentrations of intracellular K^+ in these two muscle states reportedly are the same, when expressed as concentration in noncollagenous protein nitrogen.[21] Cellular mass evidently decreases following denervation, while the mass of connective tissue, which contains much less K^+, increases.[22]

Increased K^+ efflux from normal muscle was not observed after injection of SCh. A small change was anticipated, and it is possible that this may have been within the range of control flux or might have been detectable at sampling intervals other than those used. This aspect has been studied in normal cats [22]; high values were reported for both control K^+ efflux and the post-SCh increment, but the experimental technique involved perfusion of the animal's entire hind portion, which was isolated from the cephalad portion by a pressure clamp. The authors of this report acknowledged that their perfusion techniques produced a loss of K^+. They did not report measurements of *p*H, P_{CO_2}, or muscle or blood perfusate temperatures. Although they sampled venous drainage every 30 to 60 seconds, they sampled arterial input only every 3 minutes. They then calculated K^+ efflux from the Fick formula for each 30-second interval, even though there was some disparity in the times of sampling and an un-

TABLE 3. K^+ Contents of Denervated and Normal Muscle One Hour after SCh (Five Dogs Each, Mean ± SE)

Gallamine	Muscle K^+ Content, mEq/100 g		Wet Weight, g	
	Denervated	Normal	Denervated	Normal
None	5.1*† ± 0.7	7.8 ± 0.2	49* ± 5	67 ± 4
4.0 mg/kg	7.1* ± 0.6	8.8 ± 0.3	58* ± 8	77 ± 6

* Significantly different from normal, $P < 0.05$, t test for paired data.

† Ratio of K^+ in denervated muscle to ratio in normal muscle (D/N) not significantly different from D/N at a gallamine dose of 4 mg/kg/hour, $0.05 < P < 0.1$, t test for unpaired data.

steady state [24] was present. Further studies of SCh-induced K^+ efflux in normal cats are desirable.

The $\dot{V}_{O_2}$ of denervated muscle was greater than that of normal muscle throughout the period of observation. The difference during the control period is part of an overall increase in metabolism in denervated muscle,[25] and probably is related in part to contractile activation due to fibrillation,[10] with a resultant stimulation of the Na^+/K^+ pump. In support of this assumption is the finding that resting denervated muscle [26] has a greater turnover of K^+ than does resting normal muscle. The modest increase in $\dot{V}_{O_2}$ of normal muscle after injection of SCh seems to be related to the contractile activation of fasciculations and thus represents the energy necessary to restore the contractile mechanism.

The clinical implications of these studies deserve further comment.[6] Supersensitivity to chemical depolarization develops to varying degrees within 10 to 14 days after denervation,[5] the onset of disuse leading to atrophy [27] or direct trauma to muscle.[4] The associated hyperkalemic response to SCh is well established 14 days after denervation or cord section, and it persists for about 3 months.[7] The hyperkalemic response to SCh after thermal trauma may be due not to the burn itself but to related complications. In swine, in the absence of associated direct muscle trauma or disuse atrophy, thermal trauma does not cause a hyperkalemic response to SCh [6]; in man this response frequently develops more gradually and may not be established until 21 to 25 days after the burn.[1] Therefore, hyperkalemia is more likely to be the result of atrophy secondary to prolonged bed rest and weight loss than to result from thermal trauma.

Although the degree of supersensitivity may vary with the type of neuromuscular disability, the response to SCh is such that one would expect the dose of SCh needed to paralyze normal muscles to exceed greatly that needed to depolarize the supersensitive membrane of the affected muscles, hence releasing large amounts of K^+. Gallamine and curare both attenuate the hyperkalemic response, but paralyzing doses may be necessary to block it completely. The use of SCh, therefore, probably should be avoided in patients with thermal injury, massive trauma, or lesions in the central nervous system with motor involvement resulting in atrophy.

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Respiration

LUNG LAVAGE AND DISTRIBUTION OF BLOOD FLOW Bronchopulmonary lavage was performed 16 times in nine patients with alveolar proteinosis or bronchial asthma during halothane anesthesia. In 11 lavages arterial blood gases were monitored and total shunt was calculated assuming an $A\text{-}V_{O_2}$ content difference of 4.5 ml/100 ml. In five patients pulmonary right-to-left shunt was calculated from direct measurement of arterial and mixed venous oxygen contents. In two of five patients, main pulmonary arterial, brachial arterial, and hydrostatic pressures of the liquid-filled lung were determined in addition to the cardiac output.

The arteriovenous O_2 content difference (23 measurements) was 5.12 ± 1.06 ml/100 ml. Pulmonary right-to-left shunt was above the predicted normal in every patient before lavage. It increased in every patient during lavage when one lung was filled with saline solution to a volume approaching its FRC, and it returned toward control when the lung was filled further to a volume close to total lung capacity. Also, in two patients, when the hydrostatic pressure in the liquid-filled lung equalled or exceeded the pulmonary arterial pressure, the total shunt decreased toward the control value. Cardiac output decreased appreciably in one of these two patients when airway pressure exceeded pulmonary arterial pressure. (*Rogers, R. M., and others: Hemodynamic Response of the Pulmonary Circulation to Bronchopulmonary Lavage in Man, N Engl J Med 286: 1230–1233, 1972.*) EDITOR'S COMMENT: Although the number of patients in whom the studies were made is small indeed, this is a beautiful physiologic demonstration of the relationship between lung volume and distribution of blood flow. As the liquid hydrostatic pressure exceeded pulmonary arterial pressure (or lung volume was increased from FRC to TLC), flow was diverted to the contralateral lung. This exemplifies the clinical predicament when overdistention of a small group of ventilated terminal air units may result in greater flow to nonventilated, perfused areas, thus magnifying the inefficiency of oxygenation with a simultaneous small *increase* in lung volume.