However, in rare cases, it occupies a low position and bends around the edge of the angle of the jaw, where any pressure would readily cause direct compression of nerve against bone. Possibly, the rarity of this complication lies in the rarity of this anatomic variant.

The cautionary moral in the management of this anesthetic complication concerns the "departure from usual" management simply because the patient was an esteemed physician colleague. Obviously, a really difficult or dangerous airway management problem would have been treated in this instance as in any other patient with prompt endotracheal intubation. But airway patency was not difficult to maintain provided the anesthesiologist was prepared to work harder than usual to provide anterior displacement of the jaw. In order to protect our colleague from the potential added morbidity of endotracheal intubation and the effects of a depolarizing muscle relaxant, we persisted with this well-intentioned plan. Physician patients should be treated as patients and not as physicians, and in this case early intubation would have prevented the complication described.

In summary, a patient with partial facial paralysis after general anesthesia is described. Early endotracheal intubation is called for when airway maintenance can only be achieved by strong pressure applied to the lower jaw.

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Patients with Burns Are Resistant to Atracurium

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Patients with thermal burns may demonstrate a different response than unburned patients when given muscle relaxants. Succinylcholine, a depolarizing muscle relaxant, may cause acute hyperkalemia,[1,2] whereas *d*-tubocurarine (DTC) and metocurine (MTC)—nondepolarizing muscle relaxants—have been shown to be less effective in several studies of burned patients.[3–5] As much as three times the dose of MTC used in normal subjects may be required to effect an equivalent degree of relaxation.[5]

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Atracurium is a nondepolarizing muscle relaxant with few side effects up to three times its ED_{95} of 0.2 $mg \cdot kg^{-1}$.[6,7] It has a rapid onset and short duration of action, and its elimination is independent of the kidney and liver.[8] As such, it might be a suitable alternative to succinylcholine to facilitate endotracheal intubation and maintain relaxation.

The purpose of this study was to determine the response to an intubating dose of atracurium, 0.5 $mg \cdot kg^{-1}$, in burned patients compared with that in a population of normal unburned control subjects. We also investigated the relationship between the response to atracurium and: 1) the per cent of total body surface area burned (TBSA); and 2) the number of days postburn injury.

Methods

The study was approved by the Human Studies Review Committee of the University of Washington, and oral consent was obtained from the patients. Subjects for the study were 36 (22 men; 14 women) patients scheduled for excision of burn wound or scar revision. They ranged in age from 18 to 65 yr (33 ± 2.6 yr) and in size of burn from 1% to 80% of total body surface area (TBSA). Pa-

TABLE 1. Response to Atracurium 0.5 mg · kg^{-1}

	n	Time to Maximal Depression (min)	Maximal Depression (%)	Recovery Time (min)
Control	9	3.75 ± .30	100 ± 0	45.0 ± 2.9
Before 6 days				
All sizes	7	3.18 ± .24	100 ± 0	42.28 ± 8.2
6–60 days				
less than 33%	16	4.53 ± .67	97.0 ± 2.1	42.36 ± 2.4
33–66%	7	7.54 ± 1.1*	73.5 ± 6.3*	25.00 ± 3.4*
larger than 66%	2	8.70 ± 0.1	61.2 ± 16.7	—
After 60 days				
All sizes	11	5.40 ± 0.8	95.8 ± 1.9	43.95 ± 5.4

Data are mean ± SEM.
* $P < 0.01$ compared with control.

tients with neuropathy, primary muscle disease, or those having recently received aminoglycoside antibiotics were excluded.

A control group of nine unburned patients scheduled for orthopedic surgery included six men and three women, ages 30 ± 4.1 yr. Premedication consisted of the patients regular pain medications—either methadone orally or morphine intravenously. Invasive monitoring was performed as indicated. Room temperature was elevated to help maintain patients' temperature close to their regular core temperature.

To measure the degree of neuromuscular blockade, the upper extremity was immobilized and the strength of contraction in the adductor pollicis was measured by linking the thumb to a Grass® FT10 force transducer. The ulnar nerve was stimulated *via* 22-gauge subcutaneous needle electrodes with a 0.2 ms supramaximal square wave at 2 Hz for 2 s (train-of-four). Stimulation was repeated every 12 s. The displacement was converted to an electrical signal and recorded on a strip chart recorder. Anesthesia was induced with sodium thiopental or ketamine and maintained with nitrous oxide in oxygen and fentanyl in appropriate doses. After induction, atracurium in a dose of 0.5 mg · kg^{-1} was injected in a bolus form as close to the iv site as possible. For purposes of the study the duration of blockade was timed from this point. The patient was ventilated with N_2O in O_2 until maximal twitch depression, at which time the trachea was intubated and mechanical ventilation begun. No volatile anesthetic agents were used at any time. All studies were completed before the onset of surgical bleeding. Temperature was monitored throughout the period of the study to insure stable core temperature. After neuromuscular function had returned, the strip chart was analyzed for per cent maximal twitch depression, measured as the first twitch of the train-of-four, time to maximal twitch depression, and time to return of 50% of control twitch. These data were correlated with the size of the burn (TBSA) and time from thermal injury. Data were statistically analyzed using a one-way analysis of variance and Dunnett's test of significance between means.

Linear regression and correlation coefficient were determined for twitch depression and recovery time data.

RESULTS

The nine control subjects all exhibited 100% twitch depression after the dose of 0.5 mg · kg^{-1} of atracurium. The mean time from injection to maximal twitch depression was 3.75 min, while the time to return to 50% twitch height was 45.0 min (table 1). Patients of any size TBSA burn, studied within six days postburn injury were not statistically different for any measurement, including maximal twitch depression, T_1 of train-of-four, time to maximal depression, and return to 50% control twitch (table 1).

Of those patients studied after six days postinjury and who had burns of less than 33% TBSA, only one showed less than 100% twitch depression. Their time to onset and recovery to 50% twitch were not significantly different from control (table 1).

Patients with TBSA burns of 33–66% studied after six days postinjury had only 73.5% twitch depression after 0.5 mg · kg^{-1} of atracurium and a time of onset to maximal blockade of 7.5 min, both different from control, ($P < 0.01$). The time to 50% recovery of twitch, 25.0 min, also was different from control ($P < 0.01$) (table 1).

There were only two subjects in the group of patients with burns greater than 66% TBSA who presented for surgery after six days postburn. Even though resistance to atracurium appears obvious, the small number explains the lack of a statistically significant difference.

Once the initial burn injury is healed, patients present for burn-scar revision procedures. In this group of 11 patients, it was noted that the time for maximal twitch depression, 5.4 ± 0.80 min, had returned toward control and was not statistically different from control. These patients' maximal twitch depression was 95.7 ± 1.9%, not statistically different from control (table 1). The recovery time was not significantly different from control (table 1).

In figure 1 the maximal twitch depression is plotted against the size of burn for all patients studied between 6 and 60 days postburn. Each data point represents a separate patient. The twitch depression is inversely related to the size of burn (correlation coefficient $r = -0.7045$, $P < 0.05$).

The time course of resistance to atracurium was plotted for those patients who presented repeatedly for surgery and were studied more than once (fig. 2). All four patients

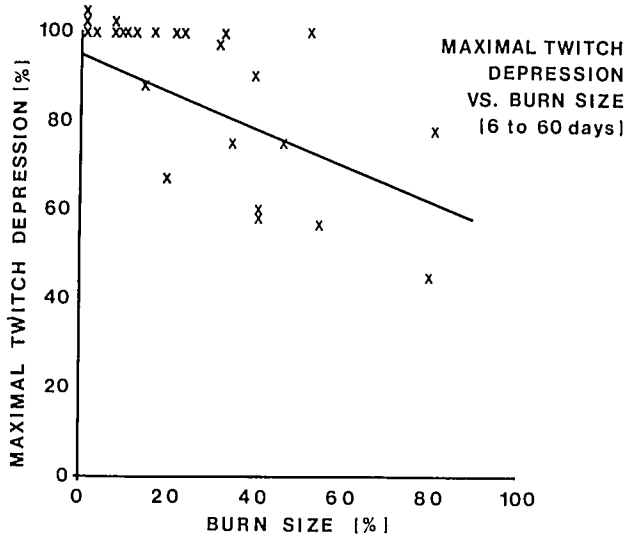

FIG. 1. Burn size *vs.* twitch depression for patients studied between six and 60 days postburn. Correlation coefficient r = −0.7045, $P < 0.05$.

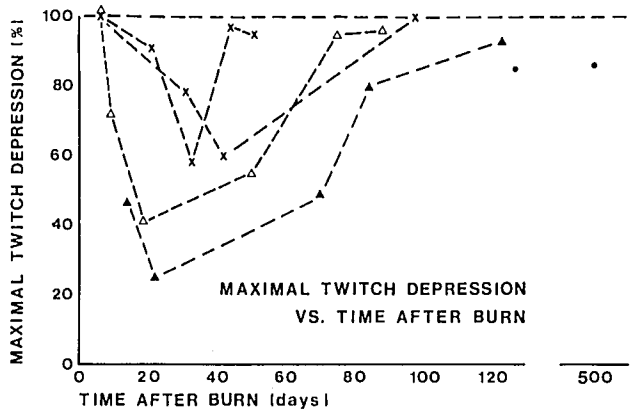

FIG. 2. Twitch depression of patients with varying burn sizes who were studied repeatedly. *Closed triangle*, 80% TBSA burn studied five times. *Open triangle*, 55% TBSA burn studied six times. *Cross*, two patients with 41% TBSA burn studied five times each. *Closed circle*, two patients studied long after their burn.

followed essentially the same time course, with the maximal resistance observed between 15 and 40 days after initial injury. Recovery from this resistance in this small patient population apeared to be related to burn size. Two patients who presented for surgery at 123 and 500 days postburn still showed less than 100% relaxation.

When the time for return to 50% twitch height is plotted against burn size (fig. 3), there is a shortened time to recovery with the increasing burn size (r = −0.6758, $P < 0.05$).

DISCUSSION

We have shown that burned patients with greater than 33% TBSA, when studied after 6 days postburn, demonstrate resistance to the effect of a 0.5 mg · kg^{-1} dose of atracurium. This is in keeping with the resistance to DTC and MTC seen by Martyn and co-workers.[3–5] Because atracurium is a shorter-acting nondepolarizing agent, we wished to assess its efficacy in facilitating tracheal intubation in the burned patient. Hence the intubating dose suggested for unburned patients, 0.5 mg · kg^{-1}, was used in a fixed dose in all patients and controls.

In their studies of DTC and MTC Martyn and colleagues gave incremental doses that allowed the construction of dose–response curves.[3–5] Administration of small increments of drug at 3-min intervals required a long-acting relaxant such that each incremental response is superimposed on a stable baseline.[9] Because atracurium is a shorter-acting agent than DTC, incremental dose experiments might yield inaccurate dose–response information. Indeed, Ørding and Skovgaard[10] and Fisher and Fahey[11] investigated incremental dose–response curves *versus* steady-state curves for vecuronium, a drug with a similar time course of activity to atracurium, and found that incremental dose–response curves were relatively high.

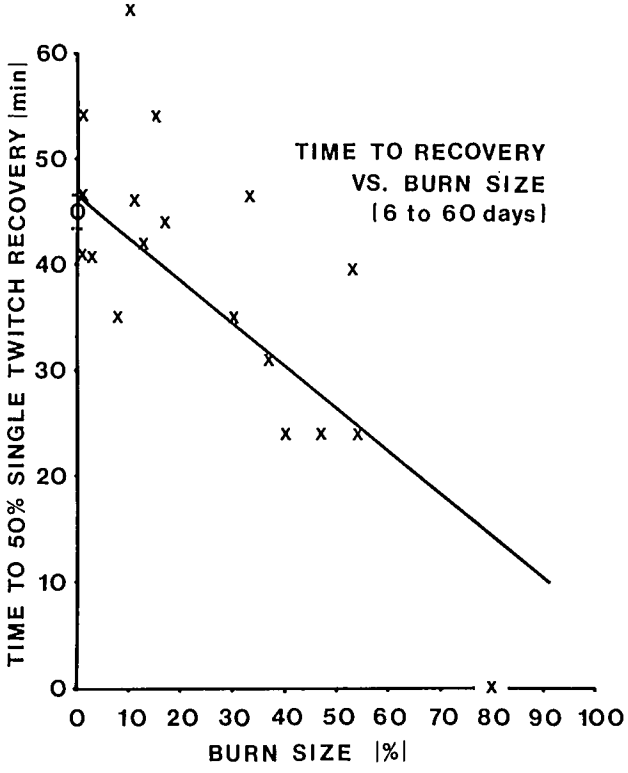

FIG. 3. Recovery to 50% twitch height *vs.* burn size, for patients studied between six and 60 days postburn. Correlation coefficient r = −0.6758, $P < 0.05$. *Open circle*, mean ± SEM for the control group. *Crosses* represent the patients.

When patients were studied after 6 days postinjury, there was a progressive decrease in paralysis that was inversely related to burn size if the burn was larger than 33% (table 1). Other studies using DTC[3] and MTC[5] show that increased dose and serum levels of drug are required to effect the same level of blockade but do not relate the degree of resistance to burn size. These studies showed increased requirements of DTC in a group of patients, one with an area burned of 25% TBSA. By using incremental doses of drug, these authors produced a degree of twitch depression less than 100% in their control patients. This may allow for more sensitive comparison between burned patients. Our dose of atracurium was designed to produce 100% twitch depression, *i.e.*, an "intubating dose." The degree of resistance in patients with less than 33% TBSA burn may have been too small to demonstrate at this larger dose. On the other hand, the pattern of resistance and dose requirements for burned patients may be different for atracurium than for DTC.

The four patients studied repeatedly showed a pattern of resistance that increased after 7 days, peaked at approximately 15–40 days, and decreased toward control by 70 days (fig. 2). It is interesting that patients studied as late as 500 days postburn still showed only 95% twitch depression after 0.5 $mg \cdot kg^{-1}$ atracurium. This pattern is similar to that reported in a single patient by Martyn and Matteo.[12]

Pharmacokinetic studies of DTC and MTC in the burned patient have demonstrated that changes in the distribution volume and protein binding of these drugs are not sufficient to account for the large differences in dose requirement and serum level.[4,5] Whether the pharmacokinetics of atracurium differ in the burned patient is unknown. If the protein binding were increased or the breakdown of drug accelerated, some degree of resistance would be noted.

Alternatively, pharmacodynamic alteration of the extrajunctional acetylcholine receptor (AChR) population, as suggested by Gronert and Theye[1] and Martyn and Szyfelbein,[3] may contribute to this resistance. There is evidence of this increase in AChR in denervated skeletal muscle, as measured by AChR ligand binding.[13] There is also evidence of resistance to nondepolarizing muscle relaxants in patients with upper motor neuron lesions,[14,15] but the state of extrajunctional AChR in these patients is unknown. Whether or how the extrajunctional AChR affects the clinical response to nondepolarizing neuromuscular blockers is unknown.

In summary, a normal response to intubating doses of atracurium is obtained in burned patients with less than 33% TBSA burn, and in patients with any sized burn less than 6 days postinjury. Patients 6 days postburn with greater than 33% TBSA thermal injury show increased requirements for atracurium proportional to the size of burn. This resistance is maximal at 15 to 40 days, is attenuated by 100 days, but some resistance may be present for as long as 500 or more days.

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