from entering the operative field. However, several small shards did manage to escape, either through the mesh or through the rear of the light assembly, and were later found on the floor of the operating room. Also, the concomitant loud noise of the explosion could have startled any member of the operating team and caused an uncontrolled motion. Fortunately, no injury resulted to the patient or to any member of the operating room team.

This case is an example of how a seemingly benign intervention during surgery, the use of a warming light, has the potential to provoke a hazardous situation even in the face of a built-in safety feature.

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(Accepted for publication January 29, 1991.)

Anesthesiology
74:960, 1991

Resistance to *d*-Tubocurarine Following Denervation

To the Editor:—I would like to offer a different interpretation of the data presented in the excellent paper by Hogue *et al.*[1] concerning denervation-induced resistance to *d*-tubocurarine (*d*Tc). The data clearly show that 1) the ED_{95} to *d*Tc is decreased in partially denervated legs; 2) the number of acetylcholine receptors (AChRs) is increased in these partially denervated muscles; and 3) there is a correlation between ED_{95} and AChR number. The seminal point of the paper, as reflected by the title, is that the increased AChR number is responsible for the resistance to *d*Tc. The discussion also cautiously indicates that factors other than increased number of receptors may contribute to the resistance. This point may have been underemphasized.

Increased AChR number is not a strong explanation for the resistance, for the following reasons. First, visual inspection indicates that the relationship between the ED_{95} and AChR number is not very strong when only the data from the affected leg is considered. The statistics presented by the author do not analyze this but rather analyze the correlation between AChR number and ED_{95} when data from control and affected limb are pooled together. Thus, an increase in receptor number in particular may not mediate the resistance but may be just one of several effects on nerve and muscle produced by partial denervation. Second, the increased receptor number is poorly correlated to the ED_{50}. Moreover, the ED_{50} is in fact not significantly changed by the partial denervation. If, as suggested by the authors, the per cent occupancy of the AChR by *d*Tc was decreased because of the increase in AChR, then the ED_{50} should be affected in the same manner as the ED_{95}. However, the data presented are inconsistent with this.

It may be that the action of partial denervation important to *d*Tc resistance is not AChR quantity but AChR quality. Following denervation, not only the number of receptors increases but also the subunit composition of the receptors changes.[2] The new denervation-induced AChRs differ from adult junctional receptors in having embryoniclike channel properties[3] and altered sensitivities to acetylcholine and *d*Tc.[2] Mediation of the resistance to *d*Tc by embryoniclike AChRs incorporated at or near the junction may explain the weak correlation to receptor number as well as the difference in effect of partial denervation on ED_{50} and ED_{95}.

Of course, other explanations for the denervation-induced resistance to *d*Tc exist. The authors (and reviewers) are to be commended for presenting results and a discussion that are open to reinterpretation.

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REFERENCES

1. Hogue CW, Itani MS, Martyn JAJ: Resistance to *d*-tubocurarine in lower motor neuron injury is related to increased acetylcholine receptors at the neuromuscular junction. ANESTHESIOLOGY 73: 703–709, 1990
2. Lorkovic H: Sensitivity of rodent skeletal muscles to dicholines: Dependence on innervation and age. Neuropharmacology 28: 373–377, 1989
3. Schuetze SM, Role LW: Developmental regulation of nicotinic acetylcholine receptors. Ann Rev Neurosci 10:403–457, 1987

Anesthesiology
74:960–961, 1991

In Reply:—We appreciate Dr. Storella's thoughtful review and appropriate comments on our report relating increased dose requirements for *d*-tubocurarine (*d*Tc) to increases in nicotinic acetylcholine receptors (AChR).[1] Dr. Storella highlights several points that deserve discussion. As he mentions, while the dose to achieve 95% twitch depression (ED_{95}) in the partially denervated animals was higher than controls, the ED_{50} between the groups did not reach significance. Likewise, while the correlation of ED_{95} and AChR was strong, the relationship was weaker for ED_{50} and AChR.

Complete denervation results in the conversion of mature to immature form of AChR. The immature differs from the mature AChR in subunit composition, binding affinities for ligands, and electrophysiologic and immunological characteristics.[2–4] The degradation half life ($t_{1/2}$) is also different. In the mature AChR the $t_{1/2}$ is ~8 days.[5] The $t_{1/2}$ accelerates

to ~3 days after complete denervation but can be decelerated back to preinnervation rate by reinnervation. The t½ of immature AChR is ~1 day. The qualitative changes occurring in our model of *partial* denervation are unknown, although our model confirms quantitative increases in AChR at 2 weeks after injury.[1] If qualitative changes do occur, the transition time for its conversion is also unknown, since this depends on the t½.[5]

In the model of partial denervation we used, we speculate that the junctional and extrajunctional AChRs affecting neurotransmission (twitch response) have a dual (mature and immature) population of AChRs. The ligand, ^{125}Iα-bungarotoxin, used to quantitate AChR, however, does not differentiate them. In contrast to α-bungarotoxin, the affinity for *d*Tc is different.[4] The affinity of *d*Tc being higher for the mature AChR, in our study low concentrations of *d*Tc may have antagonized the mature receptors only, resulting in 50% twitch depression. Inactivation of the remaining AChR, which are immature, on the other hand, would require a higher concentration of *d*Tc because of its lower affinity. Thus, the dual population hypothesis may explain the lack of difference in ED_{50} but a significant difference in the ED_{95}. Examination of the slopes of the dose-response curves indicates a significantly flatter slope ($P = 0.02$) in the denervated and suggests an altered affinity state, possibly due to a qualitative change.

Would the results be different had the experiment been performed at a later period than 2 weeks when all AChR may have been converted to the immature form? In this instance all AChRs would be resistant to *d*Tc and a significant rightward shift of the curve would occur at the lower (ED_{50}) and upper ends (ED_{95}) of the curve in addition to a flatter slope. Such a pattern was observed in the rodent burn model where the slope was flatter, and the ED_{50} and ED_{95} shifted to the right.[6] In another report on the effects of endotoxin, we observed again that ¼ LD_{50} of endotoxin shifted ED_{95} but not ED_{50} at 2 weeks, while ⅓ LD_{50} doses shifted both ED_{50} and ED_{95}.[7] Thus, the neuromuscular junctional changes may be related to both severity and duration of insult.

Relative to the second point, it should be reiterated that in the burn model too the EDs were significantly correlated with AChR number, but similar to the denervation model, a poorer correlation between ED_{50} compared to ED_{95} and AChR was observed.[6] The dual population hypothesis referred to earlier may explain this. We disagree with the approach suggested by Dr. Storella that the correlation between ED and AChR be considered for denervated group only, since this approach does not reflect the full spectrum of changes in AChR number. However, if the denervation group was studied at different times after injury, where the spectrum of changes in AChR would vary from minimal to marked, the data analysis suggested by Dr. Storella would have been possible.

In summary, our study demonstrates that partial denervation causes resistance to *d*Tc. As indicated in the discussion, an important mechanism implicated is the up-regulation of AChR. Alternate or additional and very plausible explanations include altered affinity, partial denervation-induced terminal nerve sprouting, which increases the margin of safety, and possibly altered channel properties. The relative contributions of each of these remain to be characterized.

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REFERENCES

1. Hogue CW, Jr., Itani MS, Martyn JAJ: Resistance to d-tubocurarine in lower motor neuron injury is related to increases in acetylcholine receptors at the neuromuscular junction. ANESTHESIOLOGY 73:703–709, 1990
2. Schuetze SM, Role LW: Developmental regulation of nicotinic acetylcholine receptors. Annu Rev Neurosci 10:403–465, 1987
3. Gu Y, Hall ZW: Immunological evidence for a change in subunits of acetylcholine receptor in developing and denervated rat muscle. Neuron 1:117–125, 1988
4. Beranek R, Vyskocil F: The action of d-tubocurarine and atropine on the normal and denervated rat diaphragm. J Physiol 188: 53–66, 1967
5. Shyng SL, Salpeter MM: Effect of reinnervation on the denervation rate of junctional acetylcholine receptors synthesized in denervated skeletal muscles. J Neurosci 10:3905–3915, 1990
6. Kim C, Martyn JAJ, Fuke N. Burn injury to trunk of rat causes denervation-like responses in the gastrocnemius muscle. J Appl Physiol 65:1745–1751, 1989
7. Tomera JF, Martyn JAJ. Intraperitoneal endotoxin but not protein malnutrition shifts d-tubocurarine dose-response curves in mouse gastrocnemius muscle. J Pharmacol Exp Ther 250:216–220, 1989

(Accepted for publication February 10, 1991.)

Anesthesiology
74:961–962, 1991

A Caution on the Use of Routine Depth of Insertion of Endotracheal Tubes

To the Editor:—A group of anesthesiologists at our institution use the technique of Owen and Cheney[1] of routinely securing endotracheal tubes after orotracheal intubation when the 23- or 21-cm marks are at the incisor teeth for normal adult men and women patients, respectively. However, our hospital recently changed from stocking Mallinckrodt (Glens Falls, NY) Hi-Lo polyvinylchloride (PVC) endotracheal tubes to Sheridan (Argyle, NY) PVC tubes. We initially experienced difficulty in adequately making an airtight seal by inflating the tube's cuff in several patients after orotracheal intubation using the Sheridan tubes. Direct laryngoscopy in these cases revealed that the endotracheal tube's cuff was protruding from the larynx into the hypopharynx. On comparing the two types of endotracheal tubes (fig. 1), it can be seen that the cuff on the Sheridan endotracheal tube is longer and that its proximal end is placed closer to the 15-mm adapter than is that of the Mallinckrodt tube.

Owen and Cheney[1] did not specify the type of endotracheal tube used when they described their technique of arbitrary tube placement at the incisors. Due to the variation in cuff position on endotracheal