

THEODORE A. NOEL II, M.D.
Staff Anesthesiologist
Florida Hospital Medical Center
601 East Rollins Ave
Orlando, Florida 32803

REFERENCE

1. Martin RW, Bashein G: Measurement of stroke volume with three-dimensional transesophageal ultrasonic scanning. *ANESTHESIOLOGY* 70:470-476, 1989

(Accepted for publication July 11, 1989.)

Anesthesiology
71:625, 1989

In Reply.—Dr. Noel raises an important issue regarding our paper¹ and the future growth of TEE in anesthesiology.

We agree that labor intensiveness is the single greatest impediment to wider adoption of TEE as a clinical tool. Quantitative measurements on two-dimensional images take considerable time and may require additional personnel in order to derive results in a timely fashion. The bottleneck is the time required to outline the endocardial or epicardial borders manually using a joystick or other pointing device.

We briefly discuss progress in automatic border detection of transcutaneous images in our paper. However, a recent report by Bosch *et al.** is worth mentioning as they have developed a method that appears to perform reliably and accurately on transesophageal short axis images. Further, it executes within 30 s on a microcomputer that uses the Intel 80286 processor. How well it performs on a large data set is yet to be learned.

Dr. Noel correctly points out that image processing problems such as this lend themselves to use of parallel computers. These types of computing systems do have the potential for performing border detection on-line. As an example of how technology may progress in this area, we recall struggling in the early 1970s with the computers then available to perform simple ECG analyses. Today, commercial systems

are being routinely used in Coronary Care Units to detect and analyze complex dysrhythmias in several patients simultaneously.

Our work in three-dimensional reconstruction has been undertaken in the belief that the border detection problem will be solved and come to fruition in the next several years. We therefore are investigating applications of three-dimensional cardiac reconstruction in animals and man, using tedious off-line processing while we look forward to the development of the necessary computer software and hardware to automate the process.

ROY W. MARTIN, PH.D.
Research Professor of Anesthesiology
and Bioengineering

G. BASHEIN, M.D., PH.D.
Associate Professor of Anesthesiology
Adjunct Associate Professor of Bioengineering
Department of Anesthesiology, RN-10
University of Washington School of Medicine
Seattle, Washington 98195

REFERENCE

1. Martin RW, Bashein G: Measurement of stroke volume with three-dimensional transesophageal ultrasonic scanning. *ANESTHESIOLOGY* 70:470-476, 1989

(Accepted for publication July 11, 1989.)

* Bosch JG, Reiber JHC, van Burken G, Gerbrands JJ, Gussenhoven WJ, Bom N, Roelandt JRTC: Automated endocardial contour detection in short-axis 2-D echocardiograms; methodology and assessment of variability. *Computers in Cardiology*, IEEE 88CH2733-0, 1989 pp 137-140

Anesthesiology
71:625-626, 1989

Acetylcholine Receptor Density and Acetylcholinesterase Enzyme Activity in Skeletal Muscle of Rats Following Thermal Injury

To the Editor.—The paper by Marathe *et al.*¹ tests the hypothesis that an increase in acetylcholine receptor (AChR) number explains the resistance to nondepolarizing muscle relaxants (NDMR) following thermal injury. The authors, however, find no increases in AChR number following thermal injury. Although these findings appear to contradict our previous reports^{2,3} on AChR changes following burns, certain differences in the experimental preparation used need to be emphasized in order to avoid confusion among the readers.

Our model consisted of splenectomized rat with a total body surface area (TBSA) burn approximating 45-55%.² In this model, at 10, 14, and 21 days after burn, the burned animals lost weight compared to preburn weight, which was associated with significant increase in AChR

number in the diaphragm. By 28 days, the size of the burn wound had decreased to approximately 19% TBSA, the body weight increased compared to preburn weight, and the AChR number had returned to control levels. In a more recent study,³ using the same model of 45-55% TBSA burn, the gastrocnemius response to d-tubocurarine was evaluated and correlated to AChR changes. There was a 65-225% increase in AChR in the gastrocnemius at 10, 14, and 21 days after burn and the AChR number correlated significantly with increased effective dose for d-tubocurarine ($r^2 = 0.65$, $r = 0.81$). Another study in unsplenectomized mice examined the sensitivity of the gastrocnemius muscle to d-tubocurarine, at 21 days after a 20%, 30%, and 50% TBSA burn.⁴ The effective dose of d-tubocurarine was unchanged in the

20% and 30% burn compared with controls, as was the total body weight. In contrast, the mice with 50% TBSA burn had an increase in effective dose for d-tubocurarine associated with decreases in body weight and increases in oxygen consumption. All our studies, therefore, point to the importance of burn size and the need for the continued presence of a catabolic state (weight loss) in inducing changes at the neuromuscular junction. The importance of a catabolic process induced by inflammatory mediators in producing pharmacological alterations has been reconfirmed in another pathological state: sepsis. It was observed that weight loss induced by sepsis occurred concomitantly with a rightward shift of d-tubocurarine dose-response curve while malnutrition induced weight loss was without any neuromuscular changes.⁵ Additionally, burn injury in humans results in an acute phase reactant (inflammatory) response including the release of α_1 acid glycoprotein which increases the binding of muscle relaxants.^{6,7} A rodent is also capable of an acute phase reactant response.⁸ In the rodent model studied by Marathe *et al.*, the presence of a weight loss or a catabolic process in their animals is not evident from their reports.^{1,9} The absence of a catabolic or inflammatory process in these animals is, however, suggested by the absence of alterations in protein binding to atracurium in the rodent⁹ and contrasts, therefore, with their clinical report.⁷ All these point to the inadequacy of a 30% TBSA burn in a rodent to completely replicate the clinically observed neuromuscular changes.

We also wish to take exception to the statement many times in the text that a 30% BSA burn in the rat "exhibits the distinctive time course of resistance similar to that found in burned patients: normal response to NDMR for approximately 10 days, peak resistance at 40 days, and a decline in resistance at 60 days." The clinical report¹⁰ by this group contradicts this statement. We quote from their clinical report "of those patients studied after 6 days post injury and who had burns less than 33% TBSA, only one showed less than 100% twitch depression. Their (*i.e.*, patients with burns < 33% BSA) time to onset and recovery to 50% twitch were not significantly different from control (table 1)."¹⁰ The data of table 1¹⁰ indicate no statistical difference in atracurium-induced maximal depression within 6–60 days postburn in humans who had suffered up to 33% TBSA burn. The data in table 1 are in opposition to aforementioned statement that patients with 30% TBSA burn have peak resistance at 40 days. The importance of critical burn size (usually exceeding 30% TBSA burn) in inducing neuromuscular changes has been observed in numerous studies.¹¹ With that clinical observation, one therefore wonders why a model with only a 30% TBSA burn was studied since a 30% TBSA clinically does not show resistance to NDMR.

Multiple factors may play a role in the altered sensitivity of NDMR, and may include changes in AChR number, acetylcholinesterase activity, pharmacokinetics, protein binding, and affinity of the NDMR to the AChR. In the rat model with 30% BSA burn, as suggested by Marathe *et al.*, the modest resistance to NDMR observed may well be due to the latter. There is in fact indirect evidence that there is an altered affinity between d-tubocurarine and AChR following burns evidenced by the significantly flatter and smaller slope of the dose-response curves in burned animals compared with controls.³ The re-

sistance observed with larger burns may involve all of the different etiological factors enumerated above including AChR number.

J. A. JEEVENDRA MARTYN, M.D.
Associate Professor of Anesthesiology

JOHN F. TOMERA, PH.D.
Assistant Professor of Anesthesiology
Department of Anesthesia
Massachusetts General Hospital
Boston, Massachusetts 02114

REFERENCES

1. Marathe PH, Haschke RH, Slattery JT, Zucker JR, Pavlin EG: Acetylcholine receptor density and acetylcholinesterase activity in skeletal muscle of rats following thermal injury. *ANESTHESIOLOGY* 70:654–659, 1989
2. Kim C, Fuke N, Martyn JAJ: Burn injury to rat increases nicotine acetylcholine receptors in the diaphragm. *ANESTHESIOLOGY* 68:401–406, 1988
3. Kim C, Martyn JAJ, Fuke N: Burn injury to rat causes denervation-like responses in the gastrocnemius muscle. *J Appl Physiol* 65: 1745–1751, 1988
4. Tomera JF, Martyn JAJ, Hoaglin DC: Neuromuscular dysfunction in burns and its relationship to burn size, hypermetabolism and immunosuppression. *J Trauma* 28:1499–1504, 1988
5. Tomera JF, Martyn JAJ: Sepsis but not malnutrition shifts dose-response curves to d-tubocurarine in mice. *J Pharmacol Exp Ther* (in press)
6. Leibel WS, Martyn JAJ, Szyfelbein SK, Miller KW: Elevated plasma binding cannot account for the burn-related d-tubocurarine hyporesponsiveness. *ANESTHESIOLOGY* 54:378–382, 1981
7. Marathe PH, Dwersteg JF, Heimbach DM, Pavlin EG, Haschke RH, Slattery JT: Effect of thermal injury on the pharmacokinetics and pharmacodynamics of atracurium in patients. *ANESTHESIOLOGY* 70:752–755, 1989
8. Yasuhara M, Fujiwara S, Kitade H, Katayama M, Okumura K, Hori R: Effect of altered plasma protein binding on pharmacokinetics and pharmacodynamics of propranolol in rats after surgery: Role of alpha-1-acid glycoprotein. *J Pharmacol Exp Ther* 235:513–520, 1985
9. Pavlin EG, Haschke RH, Marathe PH, Slattery JT, Howard M, Butler SH: Resistance to atracurium in thermally injured rats: The roles of time, activity, and pharmacodynamics. *ANESTHESIOLOGY* 69:695–701, 1988
10. Dwersteg JF, Pavlin EG, Heimback DM: Patients with burns are resistant to atracurium. *ANESTHESIOLOGY* 65:517–520, 1986
11. Martyn JAJ, Goldhill DR, Goudsouzian NG: Clinical pharmacology of muscle relaxants in burned patients. *J Clin Pharmacol* 26: 680–685, 1986

(Accepted for publication July 12, 1989.)

Anesthesiology
71:626–627, 1989

In Reply:—We would like to thank Drs. Martyn and Tomera for their comments regarding our paper.¹ Our findings of no increase in the density of AChR following thermal injury do contradict their findings and, as we suggested in the paper, the different findings may be related to the differences in the animal model.

The principal point of issue is the 30% TBSA rat burn model used in our study. We chose a 30% body surface area burn because it provides us a "clean burn" not complicated with factors such as sepsis, weight loss, and inactivity. Thus we have studied the role of thermal injury itself in the resistance developed to NDMR in the thermally injured