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Potential Value of Expiratory Carbon Dioxide Measurement in Patients Considered to Be Susceptible to Malignant Hyperthermia

To the Editor:—Anesthetic management of patients suspected to be susceptible to malignant hyperthermia (MH), in the absence of reliable tests to diagnose or rule out susceptibility to MH,[1] obviously should include monitoring optimal for early diagnosis of MH. Consequently, we propose that continuous monitoring of end-tidal carbon dioxide concentration offers a rapid, reliable, and noninvasive measurement of elevated carbon dioxide production, which may be one of the early clinical signs of impending MH.

Gronert and Theye found that the metabolic and hemodynamic changes with porcine MH are associated with an increase in mixed venous P_{CO_2} (Pv_{CO_2}) which is one of the early clinical indicators of the increased metabolism typical of MH.[2] In this model, high carbon dioxide production, as reflected by the rising Pv_{CO_2}, was a consistent early sign of impending MH. Furthermore, once treatment was begun, the decrease in Pv_{CO_2} seemed to indicate the effectiveness of therapy.[3]

Changes in carbon dioxide production should be reflected by corresponding changes in carbon dioxide output, as measured by end-tidal carbon dioxide concentration, provided that minute volume ventilation is constant and anesthetic depth stable. Therefore, monitoring of end-tidal carbon dioxide concentration in MH-susceptible patients could be of value for early detection of MH, and thus for early institution of proper therapy and for assessment of the effectiveness of such treatment. Monitoring of expiratory CO_2 might prove to be more reliable than, for example, body or carbon dioxide absorber temperatures, which may be relatively late signs, or an increase in heart rate, which may be caused by factors other than MH, or blood P_{CO_2} when ventilation is not constant.

We recognize that these expectations are based on data derived from the porcine model of MH, that there are only a few reports of metabolic changes in human MH.[4] Obviously only continuous monitoring of expiratory carbon dioxide concentration during anesthetic management of patients suspected to be susceptible to MH can substantiate our expectation of its clinical value.

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Conclusions Concerning "Differential Sensitivities of Nerve Fibers to Local Anesthetics" May Not Be Justified

To the Editor:—Drs. Gissen, Covino, and Gregus[1] have published a very interesting paper that I am sure will stimulate great controversy. However, their conclusion "that local anesthetic agents are similar to other biological stress modalities in terms of their differential effects on nerve fibers of various sizes and conduction velocities, *e.g.*, the large fast-conducting fibers are more susceptible to conduction blockade than are the smaller, slowing conducting fibers" is not warranted by their study. The following points should be considered when reading the Gissen *et al.* article.

Their endpoint of a 50 per cent reduction (ED_{50}) in the amplitude of compound action potentials, originated in populations of nerve fibers with greatly different speeds of conduction, is the only objective measurement to compare the effect of local anesthetics on A and C

fibers. The amplitude variations of these potentials, especially in the range chosen by the authors, are not related so much to the number of fibers responding to electrical stimulation, but to temporal dispersion in the conduction velocity of individual fibers, as discussed and demonstrated by Gasser and Erlanger,[3] Franz and Igo,[4] Paintal,[5] and Franz and Perry.[6] Slowing of this velocity (cooling in mammalian nerves, anesthetics) in the fast and usually synchronized A fibers, causes a dispersion of single action potentials with the consequent flattening and widening of the compound action potential representing this population (A wave), and little or no change in the already flat and slow C wave. Thus, "differential sensitivities of mammalian nerve fibers to local anesthetics" should be studied on single nerve fibers since the compound action potentials are limited in their resolution for this type of study.

According to Franz and Perry[6] who worked with single fibers: 1) Small myelinated axons were blocked more quickly than large myelinated axons, but this differential effect could not be accounted for by the differences in anesthetic concentration requirements. 2) The onset of block in non-myelinated axons was slower than or equal to that of small myelinated axons depending on anesthetic concentration. 3) Absolute differential block of non-myelinated (blocked) and small myelinated (not-blocked) axons was obtained by limiting the length of axons exposed to procaine to 2 mm.

Gissen *et al.* did not take into consideration the combined effects of low temperature and local anesthetics on the A fibers, known to be more vulnerable to cooling than the C fibers.[4] They performed their studies at 22°–24° C and at a stimulation frequency of 1/min in mammalian nerves (vagus and sciatic of the rabbit) which normally function at a higher temperature. To be clinically meaningful, studies concerned with the effects of local anesthetics should be related to functional depression of small fibers transmitting at their natural frequencies and temperature of operation.

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In reply: I wish to respond to the comments made by A. Galindo, M.D. concerning my article "Differential sensitivities of nerve fibers."[1]

His objections focus on three points: 1) the use of the combined action potential (CAP) amplitude does not indicate the effect of drugs on single fibers (A or C) because the peak of AP is sensitive to varying changes in conduction velocity of the component fibers. 2) Low temperature does not effect conduction in A and C fiber proportionately. 3) A stimulus frequency of 1 min is unphysiological.

His general comment is one I agree with; when possible, experiments should be performed as close to normal physiological conditions as possible. But, accurate nontraumatizing dissection of C fibers (0.5 micron or less) in lengths sufficient for *in vitro* experiments is not possible; at least not in the same manner as for A fibers (5–10 micron). We chose to use the entire nerve trunk and to "dissect" fiber behavior by conduction velocity of AP peaks.

This, of course, makes the #1 criticism important. His quotes from Franz and Perry[2] imply much more certainty than the original article warrants. I quote from page 200, "non-myelinated and small myelinated axons were blocked (0.2 per cent procaine . . .) at about the same time"; "non-myelinated axons were no more susceptible to block than were the delta and some of the smaller alpha fibers." Or in the article by Gasser and Erlanger,[3] page 588: "reconstructions were made . . . in partially blocked fibers on the assumption that the velocity in fibers of each size would be the same fraction of normal as occurs in the fastest fibers."

His quote from Franz and Iggo[4] is just as selective. Figure 4 from that article presents a graph comparing