Effect of Local Anesthetics on the Myoneural Junction

To the Editor:—A recent paper by Usubiaga and his associates (Prevention of Succinylcholine Fasciculation with Local Anesthetics, ANESTHESIOLOGY 26: 3, 1965) reports that procaine and lidocaine are capable of blocking succinylcholine-induced muscle fasciculations. This is an interesting observation (although I doubt that many physicians would care to administer 6 mg./kg. lidocaine in a 3-minute period to their patients).

Their study is significant in that it provides additional evidence that local anesthetics exert some effect on the myoneural junction. We too have recently hypothesized that local anesthetics bear a pharmacological and physiological resemblance to nondepolarizing muscle relaxants (de Jong and Wagman: Physiological Mechanisms of Peripheral Nerve Block by Local Anesthetics, ANESTHESIOLOGY 24: 684, 1963).

It would have been of interest to ascertain if the rather large doses of procaine and lidocaine given produced muscular relaxation related to their inherent myoneural properties. Furthermore, it is not clear from the description that the local anesthetics reduced the "depth" of muscular relaxation, when compared with the control group which received only succinylcholine. Was apnea observed in the treated group, for example? A rough estimate of the neuromuscular blocking effect of local anesthetics can easily be made by electrical stimulation of a peripheral nerve.

I must take exception to the authors' conclusion that local anesthetics act on the presynaptic membrane, preventing the release of acetylcholine. Since succinylcholine acts on the postsynaptic membrane (Thesleff: Mode of Neuromuscular Block Caused by Acetylcholine, Nicotine, Decamethonium and Succinylcholine, Acta Physiol. Scandinav. 34: 218, 1955), it would be difficult to understand why a block of the presynaptic membrane would prevent fasciculations.

There is additional evidence (Ehrenpreis: "Isolation and Identification of the Acetylcholine Receptor Protein of Electric Tissue," Biochim. Biophys. Acta 44: 561, 1960) to show that local anesthetics are bound to the end-plate receptor protein. It would seem clear, therefore, that the more likely site of action of local anesthetics at the myoneural junction is at the postsynaptic region.

Further study of the myoneural properties of local anesthetics seems to be required.

RUDOLPH H. DE JONG, M.D.
Associate Professor of Anesthesiology
University of Washington
School of Medicine
Seattle

To the Editor:—I greatly appreciate the interest of Dr. de Jong in our work. The aim of our investigation was to examine the inhibition of the fasciculatory action of succinylcholine by procaine and lidocaine. Therefore, we did not present any of our results dealing with the influence of local anesthetics on the depth and duration of muscular relaxation because they have been discussed elsewhere.[1]

Dr. de Jong has suggested, as Ellis [2] before him, that local anesthetics bear a pharmacological and physiological resemblance to nondepolarizing muscle relaxants. This is certainly feasible since local anesthetics drugs compete with acetylcholine for cholinergic receptors.[3, 4] However, we must also add that any muscle relaxation obtained through their myoneural action is mild indeed. Ellis,[3] for example, was unable to find any significant diminution of muscle response to electrical stimulation in cats and dogs after doses of local anesthetics six times higher than those used in our experiments.

To answer Dr. de Jong's critique of our hypothesis regarding the presynaptic site of action of the antifasciculatory effect of local anesthetics, we point out that succinylcholine has two different effects on the myoneural junction: the first and more important is blockade of neuromuscular transmission by an initial depolarization of the individual postjunctional membrane: the second, evidenced clinically by muscle fasciculations, is uncoordinated stimulation of complete nerve-motor units. Muscle fasciculations are not the result of the depolarization of the postjunctional membrane. Paton [5] has suggested two pos-

sible mechanisms for this response: muscle spindle stimulation; or, antidromal axonal repetitive firing, starting at an adjacent presynaptic membrane. After demonstrating that muscle spindles are not concerned in fasciculations,[6] Wahling concluded that retrograde stimulation of presynaptic terminals is the most probable mechanism.[7] Therefore, a logical explanation for the antifasciculatory effect of local anesthetic drugs is a presynaptic site of action. This appears to be the case, since small doses of local anesthetics diminish the presynaptic release of acetylcholine [8] and block repetitive presynaptic stimulation in doses otherwise without effect on the postjunctional membrane.[9] In other words, antidromic activation of the nerve terminals (and consequently muscle fasciculations) is more susceptible to depression by local anesthetics than orthodromic postjunctional transmission.

Since there are at least seven possible sites of action of local anesthetics on the myoneural junction, we would agree with Dr. de Jong that further study of the myoneural properties of local anesthetic drugs is certainly required.

JOSE E. USUBIAGA, M.D.
Department of Anesthesiology
University of Miami School of Medicine
Miami, Florida

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Anti-Analgesia

To the Editor:—I was very interested in your excellent and timely Editorial on the problem of pain, analgesia, and anti-analgesia. You rightly stress that some of the difficulties in this subject are semantic in origin, and in this context I wonder if you would allow me to make one small comment. You say that the term "anti-analgesia" is inappropriate since the term only describes a laboratory observation limited to tibial pain thresholds, and you suggest that "hyperalgesia" would be a better description of the effects of barbiturates. I have entirely failed to find any evidence that the barbiturates increase the appreciation of painful stimuli unless there is already some analgesia produced by a drug or some other means. The barbiturates, therefore, seem to have an antagonistic effect on the analgesic effects of other agents and it is for this reason that they have been described as anti-analgesic.

This was a new concept so a neologism seemed appropriate. I, therefore, consulted the Department of English (British English) in this University as to whether the "i" of anti should be elided, and it was on their advice that I decided on the term "antanalgesia" which you deem to be pretentious. I wonder what the term pretends other than to be a description of an observed phenomenon.

JOHN CLUTTON-BROCK, M.A., M.B., B. CHIR., F.F.A.R.C.S.
Head of Department of Anaesthetics
University of Bristol, England