Action of Lidocaine in the Central Nervous System

In this issue of the Journal, Drs. de Jong, Rolles, and Corbin present an interesting and provocative report regarding the action of lidocaine in the central nervous system. This is one of a series of papers by de Jong and his colleagues in their continuing search for the explanation of the mode of action of anesthetic agents. The report is particularly useful because, when considered with other studies, it emphasizes the complexities and difficulties involved in physiologic studies dealing with the effects of anesthetic drugs in the nervous system.

The main consideration is the possible explanation for the convulsive effect of lidocaine. Previous studies in animals have demonstrated that generalized seizures resulting from the administration of lidocaine are preceded, and possibly initiated by specific changes of electrical activity in the amygdala. The authors have interpreted their finding of enhanced monosynaptic transmission at the spinal cord level as support for the hypothesis that the excitatory effects of lidocaine may result from selective depression of inhibitory restraint on the limbic system.

However, the results of this experiment are at variance with those of Bernhard and Taverner, who found a depression of the monosynaptic reflex as well as the polysynaptic reflex over a wide range of lidocaine dosage. The explanation offered by de Jong et al. for this discrepancy deserves further thought. They emphasized that in the present study cutaneous and muscle afferents were stimulated simultaneously, while previous investigators stimulated muscle and cutaneous afferents independently. Since intravenously administered lidocaine has been shown to block conduction in nerve fibers, the authors suggest that reduction of some afferent stimuli may obscure the effects of lidocaine on synaptic transmission. This is a provocative concept, since de Jong and Nace have shown that lidocaine administered intravenously does not block large muscle afferents but only a portion of the smaller myelinated, and especially the unmyelinated fibers. However, in the present study, the authors may have not even stimulated the myelinated C fibers, the functional activity of which is not essential to the elicitation of the polysynaptic reflex as recorded. Furthermore, the nature of the synaptic blockade might be influenced by the method in which the drug was administered since this factor might be important in producing differences in plasma lidocaine concentrations as well as circulatory alterations. Although Taverner administered the drug at a relatively slow and constant rate, the method of lidocaine administration in the present study was not stated.

The authors cite the finding of Tanaka and Yamasaki that lidocaine produces preferential blockade of cortical inhibitory synapses. Although the presence of such a mechanism at the cortical level lends support to the present findings at the spinal cord, it should be mentioned that both Krenjevic and Prince have been unable to confirm these findings. Even if this particular response of the nervous system to lidocaine were well documented, it is possible that responses to lidocaine at the spinal cord level may not be the same as at higher levels. This is true for strychnine, for example, and may be true for other drugs as well. Since effects of lidocaine vary in different portions of the central nervous system, other explanations for the central action of lidocaine should be considered and explored experimentally.

It should be emphasized that the effects of lidocaine in the limbic system currently under discussion have been documented only in the cat and rabbit. Preliminary studies in our laboratory in subhuman primates have failed, so far, to demonstrate any selective action of lidocaine in the limbic system. The
extension of such relationships to man, therefore, must be done with caution.

The findings presented by de Jong et al. that significant effects of anesthetics occur at the level of the spinal cord must be considered in the overall evaluation of drug action. These considerations also apply to the inhalation anesthetics. Speculation as to the mode of action of anesthetics in the past has been based primarily on observations of neurophysiologic changes in cortical and medullary structures. Although less well studied than lidocaine, halothane also has been shown to have a distinct effect on monosynaptic transmission. In another recent report, the same authors have demonstrated that halothane significantly depresses activity of interneuronal spinal neurons, along with a decreased receptive field of cutaneous innervation. These observations indicate that significant effects of anesthetics occur at various portions of the nervous system and must be considered before we can obtain a complete understanding of the process by which anesthesia occurs.

EDWIN S. MUNSON, M.D.
Assistant Professor of Anesthesiology

IRVING H. WAGMAN, PH.D.
Professor of Physiology

National Center for Primate Biology
University of California, Davis
Davis, California

References