those induced with thiopental. In general, infants delivered following a more prolnoged period of anesthesia and surgery tended to be more acidotic and to score less on the Apgar scale at 1 minute of age. This could be due to decreased maternal perfusion of the intervillous space resulting from compression of the inferior vena cava by the uterus with the mother in the supine position, from intermittent elevation of the central venous pressure during artificial ventilation of the mother, and from surgical manipulation. A direct effect of nitrous oxide upon the fetus cannot be ruled out. Thiopental, as used in the present study, does not appear to contribute to the depression of the newborn.

Effect of Halothane and Halothane Nitrous Oxide on the H-reflex in Man. FELIX G. FREUND, M.D., THOMAS F. HORNBEIN, M.D., WAYNE E. MARTIN, M.D., and PIERRE PARMENTIER, M.D., *University of Washington School of Medicine, Seattle, Wash.* As a clinical measure of anesthetic potency, Saidman and Eger (ANESTHESIOLOGY *25:* 302, 1964) have proposed the use of the minimum alveolar concentration of anesthetic that will prevent movement in response to painful stimulation (MAC). Since anesthetics depress synaptic transmission (Brooks and Eccles: J. Neurophysiol. *10:* 349, 1947; Somjen and Gill: J. Pharmacol. Exp. Therap. *140:* 19, 1963), we sought to correlate the change in halothane MAC resulting from the addition of nitrous oxide with changes in synaptic transmission. For this purpose we studied the H-reflex, a spinal monosynaptic reflex closely related to the Achilles tendon reflex (Magladery *et al.:* Bull. Johns Hopkins Hosp. *86:* 265, 1950; Mayer and Mawdsley: J. Neurosurg. Psychiat. *25:* 201, 1965). Electrical stimulation of the tibial nerve gives rise to two contractions of the calf muscles: the first, the M-response, is due to direct stimulation of the motor nerve fibers; the second, the H-response, is due to discharge of spinal motoneurons through stimulation of the afferent nerve fibers making synaptic connection with them. *Method:* The tibial nerve was stimulated by single shocks through needle electrodes. The magnitude of the muscle contractions was measured by the amplitude of the corresponding action potentials which were recorded by means of surface electrodes and photographed from an oscilloscope. The amplitude of the H-reflex was determined before anesthesia and at end-tidal concentrations of 1.5, 0.8 and 0.3 per cent halothane with 70 per cent N_2O-O_2, and at 1.5 and 0.8 per cent halothane-O_2. In addition, at each anesthetic level the effect on the H-reflex of increasing arterial P_{CO_2} was observed. *Results:* Six volunteers have been studied. Mean amplitude of the H-reflex was 28.6 per cent of the awake response at 0.3 per cent halothane-N_2O (MAC = 1); 27 per cent at 0.8 per cent halothane-O_2 (MAC = 1); 11.3 per cent at 1.5 per cent halothane-O_2; 8.6 per cent at 0.8 per cent halothane-N_2O; and 3.8 per cent at 1.5 per cent halothane N_2O. At each anesthetic level, increasing arterial P_{CO_2} caused an additional depression of the H-reflex. Both 0.3 per cent halothane-70 per cent N_2O-O_2 and 0.8 per cent halothane-O_2 appear to be equatable in their effect on the responsiveness to noxious stimulation (as measured by MAC) and on the amplitude of the H-reflex. Assuming that the effect of nitrous oxide is simply additive to that of halothane, the results obtained at MAC = 1 mean that 70 per cent nitrous oxide is equivalent to the addition of 0.5 per cent halothane. Thus, adding 70 per cent nitrous oxide to 0.8 per cent halothane should produce the same depression of the H-reflex as 1.3 per cent halothane, but in fact that observed depression (8.6 per cent of control) was even greater than that observed in response to 1.5 per cent halothane (11.3 per cent of control). *Conclusions:* The effect of the H-reflex of adding nitrous oxide to halothane becomes more than additive as halothane concentration increases. (Supported by UW Graduate School Initiative 171 Grant, NIH Research Career Grant 5K3-HE-9617-02, USPHS Grant HE-08866-03, and a grant from the Ayerst Company.)

The Mechanism of Action of Decamethonium. A. J. GISSEN, M.D., and WILLIAM L. NASTUK, M.D., *Presbyterian Hospital and Columbia University College of Physicians and Surgeons, New York, N. Y.* Decamethanium

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(C_{10}) is no longer used routinely as a neuromuscular blocking agent in clinical anesthesiology because of its prolonged action. The later phases of C_{10} block (Phase II or desensitizing) are difficult to manage clinically. While most of the depolarizing compounds exhibit these complications to some degree, they are particularly marked with C_{10}. With the idea of learning more about the mechanisms which underlie Phase II block, we have studied C_{10} in detail. We have also attempted to reconcile some of the differences observed following C_{10} application to single cells or to whole muscle. The frog sartorius-sciatic nerve preparation was used throughout this study. *Methods and Results:* During applications of $C_{10}Br$ at various concentrations, muscle response to neural stimulation was evaluated in the isometric myograph. Potentiation of contraction without block occurred when C_{10} was applied in concentrations up to 25 μM. At concentrations of C_{10} greater than 150 μM., complete persistent neuromuscular block developed rapidly. With concentrations of C_{10} between 25–150 μM., a biphasic block appeared in which the two phases were interrupted by a transient period of recovery. The above behavior is characteristic of many of the depolarizing quaternary ammonium compounds. Electrophysiological characteristics of single cells were studied by microelectrode impalement. The initial level of membrane depolarization varied directly with the concentration of C_{10} applied. At all concentrations of applied C_{10}, resting membrane potential returned toward normal with time; the higher the concentration of C_{10}, the more rapidly this repolarization occurred. The action of C_{10} was found to be limited to the postsynaptic membrane of the neuromuscular junction. The neural action potential externally recorded at the motor nerve terminal was undiminished by C_{10}. Direct stimulation of the muscle fiber evoked a propagated action potential resulting in contraction even when neuromuscular transmission was blocked. C_{10} slowed the rate of rise of the endplate potential (Epp). Transmission failure occurred when the Epp was reduced below the critical level. From these and other experiments it can be concluded that C_{10} caused postjunctional membrane receptor activation followed by desensitization as has been demonstrated for carbamylcholine and acetylcholine (Nastuk, W. L., and Gissen, A. J.: Muscle, Eds. W. M. Paul and E. E. Daniel, Pergamon Press, Ltd., London, 1965, p. 389). *Discussion:* Although the electrophysiological effects of C_{10} parallel those produced by many of the depolarizing quaternary ammonium compounds, there are some differences. The rate at which C_{10} depolarizes the postjunctional membrane (pjm) is relatively slow. It also has a limited capacity to depolarize the pjm which cannot be overcome by increasing the C_{10} concentration. It appears that these properties of C_{10} can be explained by its prominent capacity to cause pjm desensitization. Further experiments on C_{10} desensitization are in progress. (Work performed under USPHS grants NB 04988-04; GM 00257-09; GM 09069-05, Scope E.)

Effects of Halothane on Force-velocity, Length-tension, and Stress-strain Curves of Isolated Heart Muscle. ALAN H. GOLDBERG, M.D., PH.D., *Boston University School of Medicine, Boston, Mass.* *Methods:* Studies were performed on 81 rat left ventricular cardiac preparations (69 at 25° C.; 12 at 37.5° C.), in physiologic saline solution (pH 7.35 to 7.45) gassed with carbogen (95 per cent O_2–5 per cent CO_2). Force-velocity relations were determined with an isotonic lever system by noting the initial velocity of shortening at various loads. V_{max}, P_0, "a" and "b," and the stress-strain curve of series elasticity were derived mathematically. Work was calculated as the product of the distance shortened and the load, and power as the product of the velocity of shortening and the load. Length-tension curves were obtained by plotting active developed and resting isometric tensions at increasing muscle lengths. Comparisons were made between data obtained with carbogen alone and following one hour of administration of carbogen combined with halothane (0.7, 2.0 and 3.1 vol. per cent). *Results:* The results obtained at the two temperatures were comparable in all respects. Statistically significant depressions in the force-velocity curves were observed at all halothane

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