The Effects of Muscle Relaxants and Anticholinesterases on the Neuromuscular Refractory Period in Anesthetized Man. R. A. EPSTEIN, M.D., S. R. WYTE, M.D., S. JACKSON, M.D., and S. SITTER, M.D., *National Institutes of Health, Bethesda, Md., and Walter Reed General Hospital, Washington, D. C.* The effects of minimal quantities of nondepolarizing muscle relaxants and anticholinesterases on the neuromuscular refractory period were determined in healthy adult humans maintained at a constant anesthetic depth. *Methods:* The ulnar nerve was stimulated at the elbow with single or paired supramaximal stimuli of 0.1-msec duration. The twitch tension on the adductor pollicis was recorded, and the compound muscle action potential (EMG) of the thenar eminence was displayed on an oscilloscope and photographed. The electromechanical response to paired stimulation is dependent upon the interval between the two stimuli. At intervals less than the refractory period, the response is identical to that seen with a single stimulus. The electromechanical response to paired stimulation begins to increase at a pair interval of 1.0 msec (average) and reaches a maximum at 2.0 msec (average). The "average neuromuscular refractory period" (ARP) is defined as the interval between that pair of stimuli which evokes a mechanical response equal to the average of the response to a single stimulus and the maximal response obtainable with a paired stimulus. *Results: d*-tubocurarine (0.5–1.0 mg), gallamine (5–10 mg), edrophonium (2–5 mg), and neostigmine (0.5–1.0 mg) administered intravenously had no effect on the mechanical response to a single stimulus or on the maximal obtainable response to paired stimuli. However, *d*-tubocurarine and gallamine decreased the ARP, while edrophonium and neostigmine increased the ARP. The EMG resulting from paired stimuli separated by an interval greater than the refractory period of some or all of the muscle fibers was distinguished from the single response by the presence of a second positive component in its waveform. After the intravenous administration of *d*-tubocurarine or gallamine there was an increase in the second component of the EMG evoked by paired stimuli separated by the ARP. Edrophonium and neostigmine caused decreases in this second component. The first component of the EMG was not affected. *Summary:* In man, nondepolarizing muscle relaxants decrease the neuromuscular refractory period, while anticholinesterases increase the neuromuscular refractory period.

The Effects of Germine Diacetate on the Rat Phrenic Nerve–Diaphragm Preparation. F. F. FOLDES, M.D., E. B. BRODMAN, M.D., H. N. KRANZLER, M.A., P. S. UNDERWOOD, M.D., and B. A. HENSWORTH, PH.D., *Departments of Anesthesiology, Montefiore Hospital and Medical Center, and the Albert Einstein College of Medicine, New York, N. Y.* Germine diacetate (GDA) has been employed on a limited scale in the treatment of myasthenia gravis (New Engl. J. Med. 275: 1207, 1966) and the reversal of residual neuromuscular block (ANESTHESIOLOGY 29: 850, 1968). The purpose of this study was to obtain information, under controlled conditions, about the dose–effect relationship and the time course of action of GDA and on its interaction with *d*-Tc and C10. *Results:* Concentrations of GDA ranging from 2.5 to 100.0 μg/ml caused 240 to 438 per cent mean increases in the twitch tension of the indirectly-stimulated isolated phrenic nerve–diaphragm preparations of the rat. The intensity of action of GDA was proportional, and the time required for the development of its maximal effect was inversely proportional to its concentration. Repeated administrations of GDA had progressively less and less effect. Tetanus was poorly maintained in the presence of GDA. GDA also increased the twitch tension of the directly-stimulated preparation. Muscle performance was improved by GDA during partial (40 to 60 per cent), but not during complete, *d*-Tc or C10-induced neuromuscular block. The improvement probably was due to the increase of the twitch tension of the unblocked fibers. *Summary:* These findings confirm earlier reports (J. Pharmacol. Exp. Ther. 160: 349, 1968) that the site of action of GDA is primarily postjunctional, and indicate that GDA, preferably in conjunction with anticholinester-