ence of an effective dose of a germine ester. Inspiratory force, measured as intrapleural pressure change during tracheal occlusion, was increased markedly by the alkaloids. Rapid intravenous injection caused a transient small increase in blood pressure, and a brief period of apnea followed by deepened respiratory movements. Intermittent deep inspirations when absent during anesthesia were restored by the germine acetates. *Discussion:* The experiments present evidence that partial neuromuscular block can be overcome by agents which do not act primarily on neuromuscular transmission. The germine acetates increase tension output of those muscle fibers still reached by the nerve impulse in the presence of a submaximal dose of a blocking agent. This occurs regardless of the agent used and of the nature of the existing block. An effective dose of the alkaloids increased tension output during partial or waning neuromuscular block to a level much higher than that existing before the block. One of the esters, germine diacetate, has been used in patients with myasthenia gravis where it was found to be as effective as anticholinesterase medication and, so far, free of hazardous side effects (Flacke, and others: New Eng. J. Med., *275:* 1207, 1966). *Summary:* It has been shown in cats that germine mono- and diacetate are capable of markedly increasing the development of tension in skeletal muscle in response to nerve stimulation in the presence of drug-induced partial neuromuscular block. The effect occurs regardless of the nature of the block and is presumed to be due to a postsynaptic action of the agents.

Earliest Evidence of Phase II Myoneural Block. FELIX G. FREUND, M.D., and RUDOLPH H. DE JONG, M.D., *Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington.* In man and other mammalian species succinylcholine (Sch) and decamethonium (C10) are believed to produce an initial depolarization or Phase I neuromuscular block which subsequently changes to a non-depolarization or Phase II block (Zaimis, E. J.: J. Physiol. *122:* 238, 1953). While electromyographic studies suggested that in man the transition from Phase I to Phase II occurs only after rather large doses of Sch (Churchill-Davidson, H. C., Christie, T. H., and Wise, R. P.: ANESTHESIOLOGY *21:* 144, 1960) more recent studies, measuring muscle tension, indicated that this happens with considerably smaller doses (Katz, R. L., Wolf, C. E., and Papper, E. M.: ANESTHESIOLOGY *24:* 784, 1963). In view of this discrepancy we decided to re-examine the problem of simultaneous recording of the electrical and mechanical muscle responses to nerve stimulation. *Methods:* To determine drug dosage at which transition from Phase I to Phase II block occurs we studied 32 patients anesthetized with thiopental followed by nitrous-oxide-halothane. Muscle-relaxants were administered only during the study period. Subcutaneous electrodes delivered supramaximal stimuli of 0.3 msec. duration to the ulnar nerve at the wrist. Surface electrodes and a tension transducer were used to record respectively the electrical and mechanical responses of the adductor pollicis brevis which were displayed on an oscilloscope and photographed on moving film. Magnitude of myoneural block was determined by the ratio of experimental to control response to a single stimulus. Characterization of the block as depolarization on nondepolarization was based on the commonly used criteria of constant or declining ("fatigue") response during tetanic nerve stimulation (40 stimuli per second for 5 seconds) and absence or presence of post-tetanic facilitation. Drugs were given intravenously, Sch either in single doses or continuous infusion; C10 only in single doses. *Results:* Even the smallest dose of Sch (10 mg.) or C10 (2 mg.) that would produce a measurable degree of transmission depression, invariably resulted in a nondepolarization (curare-like) block characterized by a rapid fall of both electrical and mechanical responses during tetanization, and by post-tetanic facilitation. Although typical muscle fasciculations were often noticed after the first dose of Sch and occasionally after C10, no evidence of Phase I block was seen with either drug at any time. The results indicate that in anesthetized man Sch and C10 produce a neuromuscular block that from its very onset has electro-mechanical characteristics indistinguishable from those of a curare block. (This investigation was supported by University of

Washington General Research Support Grants 11-9614 and 11-9625.)

Glucose Pool Size, Turnover Rate and $C^{14}O_2$ Production During Halothane Anesthesia in Dogs. STEPHEN J. GALLA, M.D., *University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.* Previous studies have shown that although the plasma glucose concentration is not significantly altered during halothane anesthesia in dogs, after an exogenous glucose load the plasma glucose disappearance rate is reduced (Galla, S. J., and Wilson, E. P.: ANESTHESIOLOGY *25:* 96, 1964). To define more specifically the effects of halothane anesthesia on carbohydrate metabolism, glucose pool size, turnover rate, and utilization were estimated using a radio-isotope dilution technique. *Methods:* Healthy, mongrel dogs were prepared by chronically implanting polyvinyl catheters into the aorta and right atrium through the neck vessels. When the animals resumed normal activity, studies were performed either, (1) in the conscious state, or, (2) anesthetized with halothane (1–1.5 per cent) administered through an endotracheal tube in a non-rebreathing system with 40 per cent oxygen–60 per cent nitrogen. After a 2 hour stabilization period a priming-infusion dose of glucose-U-C^{14} (90–210 mc./m*M*) was administered following the principles outlined by Steele *et al.* (Amer. J. Physiol. *187:* 15, 1956). Experiments were randomized to lessen residual effects and each dog was used as its own control. At least a 3 week interval elapsed between experiments on the same animal to insure adequate elimination of isotope. Extracellular fluid space (ECF) was measured with sulfate-35. Blood volume was calculated from the plasma volume (Evans blue) and arterial hematocrit. Glucose-C^{14} was determined by liquid scintillation after oxidation and precipitation as the gluconate. Expired $C^{14}O_2$ was trapped and counted in hyamine by liquid scintillation. Glucose pool size and turnover rate were calculated from the plasma glucose specific activity between 60–180 minutes after the beginning of the isotope infusion. Erythrocyte transketolase activity was measured by a modification of Brin's method (Brin, and others: J. Nutr. *71:* 273, 1960). *Results:* Seventeen experiments were performed on six dogs (C = conscious group; H = halothane group). During halothane anesthesia blood volume decreased slightly (C = 11.6 per cent of body weight; H = 25.5 per cent of body weight). Glucose pool size decreased significantly (C = 0.183 vs. H = 0.142 g. glucose C/kg.) as did the turnover rate (C = 0.0411 vs. H = 0.0324 g. glucose C/m.^{2}/minute). Total carbon dioxide production remained unchanged (C = 75 vs. H = 79 ml./m.^{2}/minute) but cumulative $C^{14}O_2$, expressed as a per cent of the injected dose of radioactivity expired after 180 min., increased significantly (C = 9.3 per cent vs. H = 10.8 per cent). Erythrocyte transketolase activity increased significantly after halothane (C = 2,190 vs. H = 2,360 μg./ml./hr.). *Discussion:* Reduction in glucose pool size could have been due either to decreased hepatic glucose output or increased peripheral uptake. Since turnover rate was also reduced it appears that decreased hepatic glucose output effected the reduction in pool size during halothane. The increased conversion of glucose C^{14} to $C^{14}O_2$, while the total CO_2 production was unchanged, suggested that glucose was oxidized to a greater degree during halothane anesthesia than in the conscious group. The increase in transketolase activity (an indicator of function in the pentose phosphate pathway) is in agreement with increased glycolysis. The reduction in blood volume probably resulted from sampling blood loss. *Summary:* Radioisotope studies of glucose metabolism during halothane anesthesia suggest that although the tissue uptake of glucose may be reduced a larger fraction is oxidized to carbon dioxide. There appears to be no impairment of glucose metabolism. (Supported by Grants HE-06967-05 and GM 13965-01, National Institutes of Health, Bethesda, Maryland.)

Spinal Fluid and Hyperventilation During Anesthesia in Man. BENNIE GEFFIN, M.D., *Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, Boston.* In neurosurgical anesthesia, hyperventilation is commonly employed as a means of decreasing the brain volume. This is achieved by the vasoconstrictor effect of a