ases, may be useful for the management of myasthenia gravis and the reversal of residual neuromuscular block.

The Effects of Halothane and Paired Electrical Stimulation on Isotonic Contractions of Isolated Heart Muscle. A. H. GOLDBERG, M.D., PH.D., and W. P. C. PHEAR, B.Sc., *Department of Anesthesiology, Boston University School of Medicine, Boston, Mass.* These experiments were designed to determine the effects of halothane (H) and paired electrical stimulation (PS) on resting compliance (C) of heart muscle, and to evaluate the ability of PS to improve myocardial performance in the presence of H. *Methods:* Heart muscle preparations (37 C, *p*H 7.4) from 28 rats were studied in the presence and absence of H (0.6 per cent). The contractions were isotonic and free-loaded. Changes in muscle length could be accurately detected to 10 μ. C was assessed during stretch of the muscle by a 0.75-gm load by measuring the rate of change of resting muscle length (d(l-r)/dt; direct correlation with C, with the excitation consisting of alternating 45-second periods of single stimulation (SS) and PS; or, with the mode of stimulation held constant (SS, PS, or no stimulation), by calculating Young's Modulus (force per muscle cross-sectional area per relative length change; inverse correlation with C) at ½ ($Y_{\frac{1}{2}}$) and five (Y_5) minutes following the onset of muscle stretch. *Results:* With SS, H depressed the maximum rate and extent of isotonic shortening 55 per cent and 54 per cent. PS in the presence of H restored the contractility to the level found with SS in the absence of H, but not to the higher values found with PS in the absence of H. C was increased by PS alone (d(l-r)/dt: +36 per cent; $Y_{\frac{1}{2}}$: −6 per cent; Y_5 −11 per cent), and was decreased by H with SS (d(l-4)/dt: −35 per cent; $Y_{\frac{1}{2}}$: +10 per cent; Y_5: +14 per cent). PS in the presence of H reduced C (d(l-4)/dt) 9 per cent below the value obtained with SS and H. C was reduced by H even in the absence of all muscle contractions ($Y_{\frac{1}{2}}$: +11 per cent; Y_5: +17 per cent). *Summary:* Therefore, C is increased by PS and decreased by H. Since this effect of H occurs whether the muscle is being driven by SS, whether the contractility is restored to control conditions by PS, or even if the muscle is not contracting at all, it appears that H stiffens heart muscle by a direct action on the mechanism responsible for maintenance of C.

Why Do Chronic Alcoholics Require More Anesthesia? Y. H. HAN, M.D., *Department of Anesthesiology, St. Vincent's Hospital and Medical Center of New York, New York, N. Y.* It is well known that some chronic alcoholics require greater than usual amounts of both inhalational and intravenous anesthetics. In the present study, the minimum alveolar concentration (MAC) of halothane in chronic alcoholics was determined and compared with the normal MAC. The Ostwald solubility coefficients (lambda) of halothane in homogenized human adult brain tissues from normal individuals and chronic alcoholics were compared. *Methods:* Six normal healthy adult subjects and six chronic alcoholics who had been heavy drinkers for more than ten years were studied and mean MAC values of halothane of the two groups were compared. The MAC value of halothane was determined by the technique of Eger. The lambda of halothane was determined *in vitro* in brain tissue from six normal adults and twelve chronic alcoholics and mean values for the two groups were compared. All alcoholic subjects had died from causes other than brain diseases. Histopathologic changes of the same brain tissue specimens were also observed by a neuropathologist. *Results:* The mean MAC values of halothane in chronic alcoholics were increased significantly above normal. Significant increases in the mean lambda of halothane in chronic alcoholic brain white matter to air were also observed. These increases appeared to be mainly due to decreases in CNS excitability threshold, phospholipid demyelinization, and increase in phospholipid content in the white matter of the alcoholic subjects. *Summary:* Chronic alcoholism is associated with demyelinization and increase in phospholipid content in the central nervous system. These patients require higher concentrations of anesthetics for surgery. We suggest that the inhalational anesthetic agents with lower lipid

solubilities may be preferable when general anesthesia for chronic alcoholics is required.

A New Approach to the Evaluation of Analgesics. J. C. HOFFMAN, M.D., and C. DIFAZIO, M.D., PH.D., *Department of Anesthesia, University of Virginia Medical Center, Charlottesville, Va.* Beecher and Lasagna have both emphasized that no ideal method for the evaluation of analgesic activity exists. There is a need for a method in which both the stimulus and the response are exactly measurable, which is capable of supplying dose–response data even for a weak analgesic. *Methods:* Morphine, meperidine, and pentazocine were examined, using as the measure of potency the ability of each to lower the ED50 for cyclopropane in rats subjected to a tail clamp. *Results:* Morphine (1 to 8 mg/kg body weight) and meperidine (20 to 60 mg/kg body weight) had a linearly-increasing effect. Pentazocine, on the other hand, (6 to 80 mg/kg body weight) had a ceiling effect at about 20 mg/kg body weight. Since the slopes of the dose–effect curves of pentazocine and morphine are different, no overall value for relative potency can ever be given. *Summary:* At clinically equivalent end-points, the relative potencies of the three drugs were in the ratio of morphine 1 mg, pentazocine 8 mg, and meperidine 10 mg. The dose–effect graphs for analgesia paralleled those for respiratory depressant activity in the human being (T. C. Smith, personal communication).

The Effect of Ventilation on Cerebral Oxygenation during Hypothermia. T. F. HORNBEIN, M.D., R. W. F. FORTNER, M.D., and D. C. CASSELLE, *Department of Anesthesiology, University of Washington School of Medicine, Seattle, Wash.* Although hypothermia decreases cerebral oxygen consumption, cerebral hypoxia might result from the leftward shift of the oxyhemoglobin dissociation curve, coupled with a disproportionate decrease in cerebral blood flow. Hyperventilation would enhance a hypoxic tendency because of the effect of hypocapnic alkalosis on both cerebral blood flow and oxyhemoglobin dissociation. *Methods:* Cerebral blood flow (N_2O method), cerebral venous P_{O_2}, and cerebral metabolic rates for oxygen, glucose, and lactate were determined from arterial and cerebral venous samples from 13 rhesus monkeys during halothane–curare or pentobarbital–curare anesthesia. At 37 C and 27 C, measurements were made at arterial *p*H values of 7.55, 7.40 and 7.25, produced by altering the rate of mechanical ventilation. *Results:* Cerebral oxygen consumption was 2.9 ml/100 gm/min at 37 C and 1.4 ml/100 gm/min at 27 C.

At arterial *p*H:	7.25	7.40	7.55
CBF (ml/100 gm/min) at 27 C:	72 ± 9.1	40 ± 9.7	25 ± 4.7
(± S.E.) at 37 C:	154 ± 20.7	90 ± 10.5	45 ± 5.0
Cerebral PVo_2 at 27 C:	85 ± 9.7	43 ± 3.7	27 ± 1.6
(± S.E.) at 37 C:	100 ± 4.9	72 ± 3.1	40 ± 1.2

At a given pH_a, the arteriovenous differences for oxygen were similar at both temperatures. The lower cerebral PV_{O_2} at 27 C resulted solely from the effect of temperature on oxyhemoglobin dissociation. With the limited degree of cerebral venous hypoxemia attained in this study, no indication of anaerobic metabolism was observed from the arteriovenous differences for oxygen, glucose, or lactate. (Supported by USPHS Grant He-08866 and U.W. 171 Grant 11-0560, and Career Development Award 5-K3-HE-9617-03.)