pain thresholds following intravenous doses ranging from 0.6 to 2.0 mg. ($P < 0.05$). It also decreased ischemic pain. (2) Subhypnotic doses of propiomazine neither raised the pain threshold nor disminished ischemic pain. [Supported in part by a grant from Wyeth Laboratories.]

Hypnotic Actiyity of Chloral Hydrate. FRANCES MACKAY, M.D., and JACK R. COOPER, M.D., *Section of Anesthesiology and the Department of Pharmacology, Yale University School of Medicine, New Haven, Connecticut.* When chloral hydrate is administered to man or to experimental animals, it is metabolized in the body to trichloroethanol, a potent hypnotic agent. On the basis of studies of the blood levels of chloral hydrate and trichloroethanol, Butler (J. Pharmacol. Exp. Ther. *95:* 360, 1949) and Marshall and Owens (Johns Hopkins Hosp. Bull. *95:* 1, 1954) have suggested that most, if not all, of the pharmacological effect seen after the administration of chloral hydrate is due to trichloroethanol. In the present study we have tried to correlate the degree of neurological depression with the levels of chloral hydrate and trichloroethanol in the brain. *Method and Results:* In the first series of experiments, chloral hydrate, 0.4 mg./g. body weight, was given intraperitoneally to mice. The animals were sacrificed at different time intervals after the injection and the brains were analysed for chloral hydrate and trichloroethanol. During the first 5 to 10 minutes after the injection of the drug, the neurological state of the animals appeared to be related to the concentration of chloral hydrate rather than trichloroethanol. Intravenous injections of chloral hydrate, 0.4 mg./g. body weight, in 5 mice produced a loss of righting reflex in 7 to 32 seconds. The average concentration of chloral hydrate in the brain at this time was 283 μg./g. brain, while the average concentration of trichloroethanol was only 31.1 μg./g. brain. Another series of 4 mice was given 0.04 mg./g. body weight of trichloroethanol intravenously. This dose is insufficient to produce any discernable neurological effect. These mice were sacrificed 10 seconds after the end of the injection. Although these mice showed no sign of sedation, the average concentration of trichloroethanol was 86.3 μg./g. of brain. *Comment:* These data suggest that the hypnosis observed in the mice given chloral hydrate intravenously must have been produceded by the chloral hydrate itself rather than by trichloroethanol. Thus chloral hydrate appears to be a potent hypnotic and may be responsible for the initial neurological effects after its administration. The rapid enzymatic reduction of chloral hydrate to trichloroethanol can account for the fact that previous workers have found a correlation between the blood level of trichloroethanol and the state of central nervous system depression during all but the very early stages of hypnosis after the administration of chloral hydrate.

Effects of Intrathecal Oxygen on Cortical Survival During Cardiac Arrest. WALTER H. MASSION, M.D., JOSEPH M. WHITE, M.D., *Department of Anesthesiology, University of Oklahoma Medical Center, Oklahoma City, Oklahoma.* The central nervous system is most vulnerable to acute oxygen depletion. Histologically, the gray matter of the brain is not uniformly affected by hypoxia. The earliest and most severe lesions are usually found in the pyramidal cell layer of the cortex (Courville, C. B.: Cerebral Anoxia, Los Angeles, San Lucas Press, 1953). Since these cells lie in close proximity to the subarachnoid space, an attempt was made to satisfy part of their oxygen requirement by simple diffusion from that space after the cerebrospinal fluid had been drained and substituted with oxygen. The rate of exchange between a gas pocket and the surrounding tissues is governed by Fick's first law of diffusion and depends on the solubility of the gas, the diffusion coefficient, the area of the gas tissue interface, the thickness of the cortex, and the pressure gradient of oxygen between the pocket and the tissues (Rahn, H.: Fed. Proc. *16:* 685, 1957). From standard values taken from the literature, it can be calculated that between 5 and 24 ml. of oxygen per minute will become available to the cortex depending on whether the highest or the lowest reported value for the diffusion coefficient is used. *Method:* The following experimental approach was chosen: oxygen was introduced through a frontal burrhole in anesthetized dogs at a

flow rate of 25 ml./minute and escaped freely from a needle in the cisterna magna. Radiological controls showed that unilateral filling of the subarachnoid space above one hemisphere could be accomplished if the burrhole was placed laterally from the midline. The heart was then fibrillated by electroshock applied through the closed chest wall. Comparisons between fronto-occipital EEG tracings from the right and the left hemisphere served as a basis for the evaluation of the protective effect of the oxygen depot. *Results:* In 12 dogs, electrical activity on the oxygen-supplied hemisphere survived an average of 5 minutes 46 seconds longer than on the control hemisphere. Two dogs were successfully defibrillated after seven minutes of circulatory arrest and exhibited clinical signs of unilateral brain damage with a focus on the unprotected hemisphere. Thus, it appears that introduction of gaseous oxygen into the subarachnoid space can prolong cortical survival time during circulatory arrest. [Supported by USPHS Grant B–2915 (C1).]

Infiltration of Epinephrine During General Anesthesia with Halogenated Hydrocarbons. R. S. MATTEO, M.D., R. L. KATZ, M.D., and E. M. PAPPER, M.D., *Department of Anesthesiology, Columbia University College of Physicians and Surgeons, and the Anesthesiology Service, The Presbyterian Hospital, New York, New York.* The belief that epinephrine should not be given during trichlorethylene anesthesia because severe ventricular arrhythmias may result is based mainly on experiments performed on dogs and cats in which epinephrine was injected intravenously. In this study the incidence of ventricular arrhythmias in man following subcutaneous epinephrine injection during trichlorethylene anesthesia was determined. *Method:* All patients received nitrous oxide (50–70 per cent), oxygen, and trichlorethylene through a nonrebreathing circuit. Calibrated vaporizers were used to deliver known concentrations of trichlorethylene, a maximum of 1 per cent for induction and an average of 0.3 per cent for maintenance. The electrocardiogram was observed continuosuly and direct tracings were made of any arrhythmias. Tidal volume and minute ventilation were measured with a Wright meter. Two hundred and eight patients were studied, most of them undergoing plastic surgery. One hundred and eight served as a control group. One hundred received epinephrine 1:60,000 subcutaneously in the head and neck area—a dose of 6 cc. at 5-minute intervals to a total dose of 30 cc. (500 μg). *Results:* In the control series, 6 ventricular arrhythmias occurred (5.5 per cent). Bigeminy of 45 and 50 seconds' duration was noted on two occasions. Occasional premature ventricular contractions lasting up to two minutes were seen in 4 patients. These arrhythmias followed breath-holding, coughing on the endotracheal tube and inadequate ventilation. Correction of the underlying anesthetic problem in each case resulted in a return to normal rhythm. No ventricular arrhythmias were seen in the 100 patients receiving epinephrine except for one patient in whom premature ventricular contractions lasting one and one-half minutes occurred two hours after the last injection of epinephrine. The arrhythmia occurred during hypoventilation and disappeared with improved ventilation. *Comment:* This study suggests that epinephrine in the doses stated above may be injected safely during nitrous oxide, oxygen, and trichlorethylene anesthesia provided the percentage of trichlorethylene is low (up to 0.6 per cent) and ventilation is adequate. A similar series with halothane and cyclopropane is now in progress.

Effect of Halothane on the Heart. JOHN E. MAZUZAN, JR., M.D., CALVIN HANNA, PH.D., and JOHN ABAJIAN, JR., M.D., *College of Medicine, University of Vermont, Burlington, Vermont.* Conflicting reports regarding the impact of halothane on the human heart deter or limits its use by many. Since our clinical success with halothane, based on over 15,000 cases, is difficult to reconcile with much of the published data, we examined a representative segment of our surgical population. *Method:* Our routine, relatively rigid system of administration includes alphaprodine HCl-levallorphan tartrate-scopolamine premedication followed by accurately vaporized halothane-oxygen in concentrations of 2 per cent or less. Cardiac output, which is really total tissue blood flow, was serially measured in