Oswald solubility coefficient values for halothane were: human blood (2.3), 0.9 per cent saline (0.70), pure hemoglobin (6.7), beef lecithin (126), and oil (224), giving an oil-water partition coefficient of 302. Solubility coefficients for tissue homogenates were: human kidney (3.5), liver (6.0), muscle (8.0), brain (6.0), and perirenal fat (138). Values for the corresponding beef tissues were also obtained. Comment: These results indicate the position which halothane occupies on the solubility scale of anesthetics in blood, being five times as soluble as nitrous oxide or cyclopropane and about 1½ as soluble as chloroform and 3½ as soluble as ether. With this information, we would predict that the rate of rise of the alveolar and arterial halothane tension will be slower for halothane than for nitrous oxide or cyclopropane and faster than for ether or chloroform. Values for tissue homogenates show halothane to be 1½ to 3½ times as soluble in tissue compartments as in blood. This finding is at variance with that for most other anesthetics which have a tissue/blood solubility ratio of about 1. The explanation for this difference is probably halothane’s extreme fat solubility. The increased solubility of halothane in tissues will tend to prolong both the induction and recovery time from anesthesia, beyond that occurring with agents whose tissue-blood partition coefficients approach 1.

A Study on the Analgesic Action of Propiomazine and Morphine, with a Method for Assessment of Pain in Man. H. S. Lianc, M.D., R. B. Dodd, M.D. and P. H. DeBrunne, M.D., Division of Anesthesiology, Washington University School of Medicine and Barnes Hospital, St. Louis, Missouri. We have found that propiomazine can replace a narcotic as an adjuvant in thiopental-N₂O anesthesia. This prompted us to investigate the analgesic action of this new phenothiazine derivative. Method: Normal adult volunteers were employed and tested by two techniques. (1) Pain was produced by electrical stimulation of subcutaneous sensory nerves. An electronic stimulator (Bishop, G. H.: Electroenceph. Clin. Neurophysiol. 5: 105, 1953) which delivered shocks of variable duration, frequency and intensity in the pain-stimulating range of peripheral cutaneous nerves was used. With a large metal plate serving as the indifferent electrode, a needle-electrode was inserted under the skin close to a sensory nerve of the forearm. When a current of preset duration and frequency was used, usually 2 milliseconds at 3 per second, the sensation perceived by the subject varied with the intensity. This sensation was interpreted as light touch, pressing pain or prickling pain. The latter two were used as pain end points. The number shown on the dial regulating the current intensity reflected the amount of current required for the production of each response. These numbers were recorded at two minute intervals during the control and drug test periods. Results were analyzed for significance by use of the t test.

(2) Ischemic muscular pain (Hewer, A. J., and Keele, C.A., Lancet 2: 683, 1948) was produced by a pneumatic cuff placed on the upper arm and maintained at a pressure of 220–230 mm. Hg followed by hand exercise by the subject. Exercise consisted of rhythmic compression of a bulb 60 times which produced a deep aching pain of increasing degree in the forearm and hand. The pain could be graded as slight, moderate, severe, very severe and intolerable. There were no clear end points, but the degree of pain could be plotted against time and usually showed a linear pattern. The inflatable cuff was released at the end of fifteen minutes. All grades of sensations were reported verbally by the subject. An intravenous infusion was started prior to each experiment. A five to ten minute period was usually required to provide a steady state of response to a given stimulation. The use of the two techniques simultaneously did not interfere with the results from either, as shown in our control series. Three coded solutions were used. Neither the tester nor the subject knew which solution was given. The solutions were normal saline, as placebo, morphine 0.4 mg. per cc. and propiomazine 4 mg. per cc. Five subjects completed the series of tests. Each subject received a different amount of each solution at a different time. An interval of one week was allowed between tests. Results: By comparing the means taken prior to and after the injection of the drug in each series, we observed the following: (1) Morphine produced significant elevations of both

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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 diminished ischemic pain. [Supported in part by a grant from Wyeth Laboratories.]

Hypnotic Activity of Chlortal 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 chlortal 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 chlortal 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 chlortal hydrate is due to trichloroethanol. In the present study we have tried to correlate the degree of neurological depression with the levels of chlortal hydrate and trichloroethanol in the brain. Method and Results: In the first series of experiments, chlortal 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 chlortal 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 chlortal hydrate rather than trichloroethanol. Intravenous injections of chlortal 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 chlortal 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 discernible 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 chlortal hydrate intravenously must have been produced by the chlortal hydrate itself rather than by trichloroethanol. Thus chlortal hydrate appears to be a potent hypnotic and may be responsible for the initial neurological effects after its administration. The rapid enzymatic reduction of chlortal 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 chlortal 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