absorption was illustrated by the procaine concentration of 1.09 μg./ml. achieved 30 seconds following injection of 1 ml. of 2 per cent solution. The absorption curves resulting from 1 ml. each of a 1 per cent and 2 per cent procaine solution, did not demonstrate a linear relationship during the initial five minute absorption period. The concentrations resulting from the 2 per cent solution far exceeded the linear increase expected due to the larger dose administered. This increase was due possibly to the vasodilating property of procaine. The addition of 1:100,000 epinephrine to a 2 per cent solution effectively retarded absorption, but the minimal initial effect may have been due to the vasodilating potential of low concentrations of epinephrine.

Central Nervous Actions of Halothane Which Affect the Circulation. H. L. PRICE, M.D., H. T. MORSE, M.D., and H. W. LINDE, PH.D., *Department of Anesthesia, University of Pennsylvania Schools of Medicine, Philadelphia, Pennsylvania.* The cause of arterial hypotension during halothane administration has been attributed by various authors to ganglionic blockade, direct actions on vascular smooth muscle, myocardial depression, and actions exerted within the central nervous system. None of the suggested mechanisms has actually been shown to operate; consequently it is not known which, if any, of the suggestions is correct. *Method:* In the experiments to be described, halothane was administered to the cephalic circulation of dogs while effects on the systemic circulation were recorded. Circulation to the head was supplied by a pump-oxygenator. Heparin was used to prevent coagulation. The blood was perfused through the brachiocephalic artery and collected from the superior vena cava downstream from the point of entry of the azygos vein. To provide anesthesia for the necessary surgical operations chloralose was given intravenously in small (50–70 mg./kg.) dose. Halothane in oxygen was supplied to the oxygenator when desired by means of a vaporizer. A Beckman infrared analyzer sampling expired air by the microcatheter technique was used to detect contamination of the systemic circulation with halothane. The limit of sensitivity of this instrument was 0.05 per cent halothane. In no experiment was contamination detected. *Results:* Preliminary findings were that halothane could produce all of its characteristic actions on the systemic circulation when its distribution was confined to the head. Measured changes included diminished carotid sinus reflex, arterial hypotension, reduced myocardial contractile force, and bradycardia. Most or all of the changes appeared to result from reduced sympathetic nervous discharge.

Reflex Activity of the Larynx During Breathing. C. C. RATTENBORG, M.D., M. D. BARTON, M. L. KAIN, W. J. LOGAN, H. R. KONRAD, and D. A. HOLADAY, M.D., *Section of Anesthesiology, University of Chicago School of Medicine, Chicago, Illinois.* The larynx participates actively in breathing. The normal laryngeal reflexes open the larynx during inspiration. This pattern was observed in a large number of dogs anesthetized with either pentobarbital or halothane. *Method:* The present study included five dogs. The respiratory airflow was monitored by a pneumotachograph connected to a tracheotomy tube. The laryngeal resistance to airflow was recorded continuously as the translaryngeal pressure gradient caused by a constant flow of air being passed through the larynx. Electromyograms (EMG) were obtained with platinum wire electrodes. Inspiratory activity during quiet breathing was obtained most consistently from the middle constrictor, which was demonstrated to be a laryngeal "opener" by electrical stimulation. Electromyograms of the ala nasi and the diaphragm were also obtained. The time pattern of the events was related to the moment the airflow started. *Results:* Activity of the ala nasi preceeded the airflow by 50–150 milliseconds. The diaphragm started 0–50 milliseconds before the airflow. In the normal dog EMG activity in the middle constrictor started 0–150 milliseconds after the flow, but before an appreciable flow was achieved. The time pattern was observed to be unaltered from very light anesthesia (halothane 0.25 per cent) to deep anesthesia (3 per cent). The pattern on EMG intensity was related to depth of anesthesia. The activity in the diaphragm decreased with increasing depth of anesthesia as did the respiratory airflow. The ala nasi muscle showed a practically unchanged ac-

tivity. The activity in the middle constrictor increased with increasing depth. At a very deep level a decreased activity was observed; but even the last breath in deep anesthesia showed electromyographic activity. *Conclusions:* Because of a practically unaltered time sequence of activation it is assumed that unaltered central pathways were available for the individual muscles when anesthesia was deepened. Because no parallelism was observed in the responses of these motor functions to changes of depth of anesthesia, it can be tentatively concluded that each depends on a different, though related, central regulatory mechanism. [This work was supported in part by a grant from the Burroughs Wellcome & Co. Inc. The Fluothane used in this study was provided by Ayerst Laboratories.]

Effect of Reserpine on Cardiac Function During Thiopental-Cyclopropane Anesthesia. B. F. Rusy, M.D., M. R. Wester, M.D., K. Shetty, M.D., E. Freeman, B.A., and L. W. Krumperman, M.D., *Departments of Anesthesiology and Pharmacology, Temple University Medical Center, Philadelphia, Pennsylvania.* The direct, depressant action of cyclopropane on the heart is not overtly demonstrated in the intact organism because, as suggested by Price and others, this agent causes the release of norepinephrine which has a positive inotropic effect on the myocardium. Reserpine depletes cardiac tissue of its norepinephrine content and Blinks and Waud have demonstrated that pretreatment with reserpine effectively blocks the positive inotropic effect normally caused by stimulation of the cardiac accelerator nerves. It might therefore be expected that reserpine pretreatment would unmask the direct depressant effects of cyclopropane on the heart. Clinical evidence in support of this possibility has emerged in case reports describing cardiovascular collapse following anesthesia in reserpinized patients. A study of the effect of reserpine pretreatment on cardiac function during anesthesia induced with thiopental and maintained with cyclopropane is currently being carried out in dogs. *Methods:* Cardiac function was evaluated by measuring the cardiac output (dye-dilution) and the rate of rise of left ventricular pressure during the isometric phase of systole. The latter measurement was obtained by differentiating the electrical analog of left ventricular pressure and is, according to Rushmer, an index of myocardial "contractility." These two parameters plus heart rate and mean arterial blood pressure (MABP) are measured in the unanesthetized animal and compared with similar measurements made following 45 minutes of thiopental-cyclopropane anesthesia. Experiments on each animal are done before reserpine and following each of three successive reserpine treatments which consist of: (1) reserpine 10 μg./kg./day $\times$ 10, (2) reserpine 20 μg./kg./day $\times$ 5, and (3) reserpine 100 μg./kg./day $\times$ 1. Cyclopropane 25 per cent in O_2 is administered by nonrebreathing technique such that equal end-expired cyclopropane concentrations are maintained in the pre- and post-reserpine experiments. Respirations are controlled and the P_{CO_2} is held within the normal range. *Results:* To date, five dogs have been carried satisfactorily through the study. Reserpine in all doses caused a decrease in heart rate, MABP and left ventricular "contractility" in the unanesthetized animals. Cardiovascular collapse following anesthesia did not occur in any experiment, even after the high dose of reserpine. Changes caused by anesthesia are expressed as the average of the percentage changes from the unanesthetized values for each experiment and are as follows: Heart rate and MABP increased 30 per cent and 5 per cent respectively, while "contractility" decreased about 30 per cent, both before and after reserpine; *i.e.*, reserpine exerted little or no effect upon the per cent change caused by anesthesia in these parameters. Following anesthesia before reserpine, cardiac output fell an average of 13 per cent below the awake value. After reserpine, cardiac output was depressed more severely by anesthesia. In those animals who had received the high dose of reserpine, the average decrease below the awake value was 37 per cent. Whether this decrease is significantly greater than the decrease before reserpine is not known at present. *Conclusions:* The findings indicate that reserpinization of the normal dog does not severely inhibit his ability to compensate for the cardiovascular depressant effects of thiopental-cyclopropane anesthesia.