ysis of data curves using mathematical methods which, to our knowledge, have not heretofore been used in biological research. The system can be applied to any data from transducers or other measuring devices, the output of which varies with time.

Systemic Absorption of Procaine Following Submucosal Injection. JAMES R. OOSTING, D.D.S., LEONARD M. MONHEIM, D.D.S., and STEPHEN J. GALLA, M.D., *Department of Anesthesiology, Graduate School of Dentistry and School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania.* The relation between the absorption rate of local anesthetic agents and undesirable physiological responses has long been recognized. Allen and Livingston (Anesth. Analg. *21:* 285, 1942), Overgaard (Acta Pharmacol. Toxicol. *1:* 153, 1945), and Maykut (Canad. Anesth. Soc. J. *6:* 160, 1959) investigated peripheral venous blood levels of procaine following subcutaneous injections. Adriani and Campbell (Anesth. Analg. *38:* 370, 1959; J. A. M. A. *168:* 873, 1958) have done extensive studies of absorption following topical, intravenous, subcutaneous and intraperitoneal administration. The aforementioned investigators determined the peripheral venous concentration of local anesthetic agents at various intervals following administration. These investigators apparently assumed that no significant differences existed between peripheral venous, central venous, and arterial concentrations. Previous studies have not fully explored the absorption rate following subcutaneous injections. Consequently, additional studies of absorption of local anesthetic agents appeared justified. *Methods:* To obtain samples of mixed systemic venous and arterial blood in dogs, polyvinyl catheters were inserted permanently into the right atrium through the right external jugular vein and into the ascending aorta through the right common carotid artery. Catheter position was verified radiographically. Following recovery from the operative procedure, experiments were performed under pentobarbital anesthesia. Following control sampling, 1 ml. of the test solution was injected submucosally above the right maxillary cuspid tooth over a 30-second period. A 2-ml. blood sample was taken immediately, and at intervals of 30 seconds, 1, 3, 5, 15, 30, 45, 60, and 90 minutes. Four solutions were used: 1 and 2 per cent procaine; 2 per cent procaine with 1:50,000 epinephrine, and 2 per cent procaine with 1:100,000 epinephrine. Using internal standards, samples were analyzed by a modification of the Kisch-Strauss method (Exp. Med. Surg. *1:* 66, 1943). *Results:* Following injection of 1 ml. 2 per cent procaine, the mixed systemic venous and arterial blood concentrations of procaine were identical during the 90-minute period, but they differed significantly from concentrations in femoral venous blood. The procaine concentrations 30 seconds following injections were 0.99 μg./ml. in mixed systemic venous blood and 0.13 μg./ml. in femoral venous blood. At one, three, and five minutes, the concentrations in mixed systemic venous blood were 1.42, 1.85, 2.21 μg./ml., compared to 0.47, 1.00, 1.35 μg./ml. in femoral venous blood. The maximum mixed systemic venous concentration of 3.37 μg./ml. (30 minutes) did not differ significantly from the peak of 3.30 μg./ml. (45 minutes) in femoral venous blood. The procaine concentrations from the three sources were nearly identical at 90 minutes. Using 1 ml. each of a 1 and 2 per cent solution, the concentration 30 seconds following injection of the 2 per cent solution was nearly five times that of the 1 per cent solution. The concentrations from the 2 per cent solution remained more than twice those of the 1 per cent solution throughout the first three minutes following injection. Thirty seconds following injection of 2 per cent solution with 1:100,000 epinephrine, the concentration was 0.74 μg./ml., which was not significantly different from the 0.99 μg./ml. obtained with 2 per cent solution without epinephrine. The 1:50,000 epinephrine solution resulted in a concentration of 0.15 μg./ml. 30 seconds following injection. Significant reductions in blood concentrations were obtained with both 1:50,000 and 1:100,000 epinephrine solutions during the remaining 60 minutes *Comment:* The results demonstrated the important differences in blood concentrations of procaine, depending upon the sampling site employed. Critical selection of the blood sampling site appeared essential in studies on absorption of local anesthetic agents The initial speed of

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-