thiopental anesthesia. All patients received 100 mg. of pentobarbital and 0.4 mg. of scopolamine as premedication, and underwent the same operation, dilation and curettage. Arousal and awakening times were recorded. The former was when the patient responded to painful stimuli, moved, and opened her eyes; the latter, when she responded coherently to questions. The control group received an average dose of thiopental of 500 mg.; average operation time, 38 minutes; average arousal time, 21 minutes, and awakening time, 23 minutes. In the group receiving 50 mg. of Vandid, at the end of operation, the average dose of thiopental was 550 mg., average operation time, 20 minutes; average arousal time, 6 minutes, and average awakening time was 23 minutes. In the group receiving 75 mg. of Vandid at end of operation, the average dose of thiopental was 500 mg.; average operation time, 20 minutes; average arousal time, 7½ minutes, and average awakening time, 9 minutes. Coughing and sneezing were noted in a small percentage of patients in this group. In the group receiving 100 mg. of Vandid at completion of operation, the average dose of thiopental was 470 mg.; average operation time, 20 minutes; average arousal time, 8 minutes. Almost all of these patients showed severe side effects such as flushing of the face, sneezing, coughing and some stiffness of the extremities.

The Influence of Ganglionic Blockade and Vasopressor Drugs on the Elimination of a Waterload and on the Histologic Appearance of the Kidney. ANTONIO BOBA, M.D., AND ARTHUR A. STEIN, M.D. *Departments of Anesthesiology and Pathology, Albany Medical College of Union University, Albany, New York.* This study attempted to evaluate changes in the kidney parenchyma from the administration of a vasopressor drug capable of inducing prolonged vasoconstriction. The ability of reflex vasoconstriction to produce histologic changes attributable to local anoxia has been investigated (*Boba, A.; Powers, S. A., Jr.; Stein, A. A.: Anesthesiology 20: 268, 1959*). Adult, splenectomized, mongrel dogs were used. After induction of anesthesia with intravenous pentobarbital, one femoral artery and vein were cannulated. Both ureters were cannulated through a median laparotomy incision, and after a control period of thirty minutes the experiment was begun. Over a period of two hours, a volume of 2.5 per cent glucose in water with 0.5 normal saline equal to 20 per cent of the weight of the animal, was injected into the control dogs. Checks of the injected volume and of the urinary output were done every fifteen minutes. At the end of the experiment a complete autopsy was performed on each animal. Two additional groups were investigated, the first group given l-norepinephrine and the second, camphorsulphonate (Arfonad), via a second venous cut down. The diluent fluid was the same as in the controls, and the rate of administration adjusted so that the total waterload was the same. The administration of l-norepinephrine increased the systemic pressure to 160 per cent of control values, and camphorsulphonate decreased the systemic pressure to 50 per cent of control values. These animals were also sacrificed after two hours. In the control group the urinary output increased moderately during the period of observation, there were no noticeable changes in the blood pressure and no abnormalities were observed in the histologic appearance of the kidney. The group subjected to ganglionic blockade with camphorsulphonate showed a somewhat reduced urinary output when compared with the control, the blood pressure remained low and the kidneys appeared normal except for some vacuolization of the tubular cell cytoplasm. However, if the pressure had been lowered below 50 mm. Hg systolic, these changes were more pronounced and occasionally disorganization of the cellular architecture was seen. The group treated with l-norepinephrine exhibited a pronounced increase in urinary output during the first 75 to 90 minutes, after which time it practically disappeared. At this time the blood pressure could be maintained elevated only by continuously increasing the concentration of the drug. The histologic appearance of the kidney showed tubular cellular changes limited to the cellular architecture without apparent tissue alterations. The reversibility of the observed changes was also evaluated. In this series, the control animal recovered well from the acute experiment, and did not show significant renal alterations after

72 hours. There were no survivors in the group treated with l-norepinephrine, all deaths occurring within one hour after termination of the acute experiment. Immediate autopsy revealed collections of clear fluid in the pericardial and pleural cavity, conspicuous edema of all soft tissues and pronounced engorgement of the small bowel's vasculature. The conclusion may be drawn that the simultaneous administration of a large volume of fluid and vasopressor (l-norepinephrine) to the normovolemic animal is not tolerated. Furthermore, recent reports on the adverse effects of the administration of the same vasopressor in the experimental animal have been indirectly confirmed. [*Supported in part by a grant from Hoffmann-La Roche Inc., Nutley, N. J.*]

Clinical Investigation of Local Anesthetics: Evaluation of Chloroprocaine (Nesacaine) by the Double Blind Method. John J. Bonica, M.D., Nobuo B. Nishimura, M.D., Van S. Lawrence, M.D., and David N. Goodson, M.D. *Department of Anesthesiology, Tacoma General and Mt. View General Hospitals, Tacoma, Washington.* The present trial was part of a study to assess local anesthetics for clinical use. It concerns 195 cases of extradural anesthesia performed under clinical conditions in an attempt to evaluate chloroprocaine (Nesacaine) with procaine as the standard agent. Lidocaine (Xylocaine) was also studied. The principles previously described (*Bonica, J. J., Anesthesiology 18: 110, 1957*) were adhered to. The drugs were dispensed as unknowns according to previously prepared random tables and the investigators followed standardized procedure. The volume of the solutions was kept constant, 15 ml. being injected for lumbar peridural block and 25 ml. for caudal anesthesia. The properties of local anesthetics studied included (1) latency of time of onset; (2) penetrance or spread of solution; (3) duration of block; and (4) toxicity. Pain sensation was tested by pin prick; a dull sensation was interpreted as hypalgesia; loss of pin sensation in the presence of pressure sensation as analgesia; and complete absence of sensation as anesthesia. The time of onset of sensory changes at T10 level on each side was noted and a complete survey was made fifteen minutes after injection. The onset of partial and complete loss of leg-raising was used as an index of motor block. Penetrance was assessed by degree and evenness of spread of the local anesthetic. A difference in either analgesia or anesthesia of three or more segments between each side was considered to be uneven spread. The value of each block was assessed; with the technique described, a useful concentration of local anesthetic was defined as that concentration which spread evenly to provide T10 analgesia in 15 minutes. Each case was recorded on a special form. Upon completion of each series, the results were tabulated as absolute frequencies, and the tables subjected to statistical analysis. To date, the completed studies include (1) a pilot study of 75 cases; (2) a series of 48 cases in which chloroprocaine was compared with procaine; and (3) 72 cases comparing lidocaine, chloroprocaine and procaine.

Procaine in concentrations ranging from 2 to 4 per cent produced a high rate of partial or incomplete block. Subsequently, 3 per cent chloroprocaine was evaluated with 4 and 5 per cent procaine. These data revealed the onset of analgesia and anesthesia with 3 per cent chloroprocaine was significantly shorter than with 4 per cent procaine. The data on duration of anesthesia revealed no significant difference between the two solutions. Chloroprocaine was significantly more penetrant than 4 per cent procaine, but 4 per cent procaine produced significantly higher incidence of minimal toxic reactions. Data concerning 5 per cent procaine and 3 per cent chloroprocaine revealed no significant difference between the two drugs as far as onset of analgesia and anesthesia, duration, penetrance, and degree of muscular relaxation. One patient who received 5 per cent procaine developed marked toxic reactions. It was concluded that 3 per cent chloroprocaine is superior to less than 5 per cent concentrations of procaine. Although 5 per cent procaine is as effective as 3 per cent chloroprocaine, this preliminary study indicated that it was more toxic. The data concerning evaluation of chloroprocaine, lidocaine and procaine revealed the following: chloroprocaine and lidocaine showed a significantly shorter time of onset than procaine. There was no statistical difference between chloroprocaine and lidocaine. Both drugs showed greater penetrance