

some patients (Kimmey, J. R., and Siebecker, K. L.: to be published). Lidocaine also increases the duration of apnea produced in dogs by succinylcholine (DeKornfeld, T. J., and Steinhaus, J. E.: *Anesth. & Analg.* 38: 173, 1959). In patients anesthetized with nitrous oxide and thiobarbiturates, the administration of lidocaine intravenously did not produce the depression of blood pressure noted when procaine was similarly given (Kimmey, J. R., and Steinhaus, J. E.: *Acta anaesthesiol. scandinav.* 3: 9, 1959). The technique of Jolly and Steinhaus (*J. Pharmacol. & Exper. Therap.* 116: 273, 1956), by which drugs can be administered to a limited portion of the brain through the vascular supply, was used in this study to demonstrate the effect of lidocaine on the central nervous system. Ligation of the basilar artery of the rabbit separates the circulation of the internal carotid and vertebral arteries, allowing the administration of drugs to centers of the brain above or below this level. (Convulsions occurred when cocaine was injected into the internal carotid artery, but severe depression of medullary centers resulted from injection into the vertebral artery. Lidocaine in doses of 0.125, 0.25, 0.5 and 1.0 mg./kg. of body weight were injected into the femoral vein, carotid artery and vertebral artery of rabbits so prepared. Injection into the carotid artery produced muscular movements or convulsions in most animals. Injection into the vertebral artery produced respiratory changes, and in 9 of the 25 rabbits apnea occurred. Circulatory changes were inconsistent and often delayed in onset, suggesting that they may have been due to direct action on the circulatory system rather than from central nervous system effect. These experiments have shown that lidocaine injected into the vertebral artery in rabbits can produce respiratory depression and apnea, presumably as the result of action upon medullary centers. Convulsive activity and muscle movements were also produced, most often when the drug was injected into the carotid artery.

**Respiratory Effects of Phenazocine (NIH 7519, Prinadol) and Morphine.** J. WELDON BELLVILLE, M.D., STANLEY L. WALLENSTEIN, M.S., RAYMOND W. HOUDE, M.D., AND WILLIAM S. HOWLAND, M.D. *Department of*

*Anesthesiology, Memorial Center for Cancer and Allied Diseases and the Section of Experimental Anesthesia, Division of Experimental Surgery, Sloan-Kettering Institute, New York, New York.* The respiratory depressant effects of phenazocine and morphine were evaluated in 5 healthy male subjects. Respiratory depression was defined in terms of displacement of the alveolar ventilation-alveolar  $P_{CO_2}$  response curve (Seed, J. C., et al.: *Arch. internat. pharmacodyn.* 116: 293, 1958). A modification of the rebreathing method of Eckenhoff, Helrich, and Hege (*Anesthesiology* 17: 66, 1956) was employed, and the alveolar ventilation- $P_{CO_2}$  response curve was obtained automatically with the aid of an analog computer (Bellville, J. W., and Seed, J. C., *Science* 130: 1079, 1959). Morphine sulfate was administered intramuscularly at the 5 and 10 mg. dose level (two subjects received 7 mg. instead of 5 mg.) and phenazocine was studied at the 1.5 and 3.0 mg. dose level. The mean displacements and doses are as follows: morphine 5.8 mg.—3.42 mm. Hg, morphine 10 mg.—5.87 mm. Hg, phenazocine 1.5 mg.—5.74 mm. Hg, phenazocine 3.0 mg.—8.97 mm. Hg. From these data phenazocine was estimated to be 6.4 times as potent as morphine in terms of their effects on respiration.

**Effect of Vanillic Diethylamid (Vandid) on Arousal and Awakening Time Following Thiopental Anesthesia.** MELVIN L. BERNSTINE, M.D., AND JOSEPH P. MOSKAL, M.D. *Department of Anesthesiology, Albert Einstein Medical Center, Philadelphia, Pennsylvania.* Vandid, the diethylamide of vanillic acid, has properties similar to Coramine, the diethylamide of nicotinic acid. In animals, intravenous injection is followed by a transient apnea (prevented by vagal blocking), followed by a two or three-fold increase in depth of respiration. Blood pressure falls transiently before a sharp rise of short duration. In man, the respiratory effects are similar; however, there is no effect on blood pressure unless it is below normal, in which case it usually returns to normal levels. This drug alone has been used to treat 8 cases of severe barbiturate intoxication. Six of the 8 patients recovered within twelve hours or less. A study was made of the action of Vandid following operation using

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