

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 Chlorprocaine (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 chlorprocaine (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 chlorprocaine was compared with procaine; and (3) 72 cases comparing lidocaine, chlorprocaine 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 chlorprocaine was evaluated with 4 and 5 per cent procaine. These data revealed the onset of analgesia and anesthesia with 3 per cent chlorprocaine was significantly shorter than with 4 per cent procaine. The data on duration of anesthesia revealed no significant difference between the two solutions. Chlorprocaine 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 chlorprocaine 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 chlorprocaine is superior to less than 5 per cent concentrations of procaine. Although 5 per cent procaine is as effective as 3 per cent chlorprocaine, this preliminary study indicated that it was more toxic. The data concerning evaluation of chlorprocaine, lidocaine and procaine revealed the following: chlorprocaine and lidocaine showed a significantly shorter time of onset than procaine. There was no statistical difference between chlorprocaine and lidocaine. Both drugs showed greater penetrance

than procaine. The segments of spread for chlorprocaine and lidocaine was approximately the same, but lidocaine produced a significantly greater evenness of spread. This suggests that lidocaine is more penetrant than chlorprocaine. The duration of anesthesia was significantly greater with lidocaine than with both chlorprocaine and procaine. No serious toxic reactions occurred in the second phase of study. Procaine and chlorprocaine produced a slightly greater incidence of minimal toxic symptoms, such as tinnitus and slight nausea, than lidocaine. Further studies are planned to enlarge the samples and to include other agents.

An Assessment of Respiratory Efficiency in the Postoperative Patient. JOSEPH J. BUCKLEY, M.D., AND FREDERICK H. VAN BERGEN, M.D. *Department of Anesthesiology University of Minnesota Medical School, Minneapolis, Minnesota.* Hamilton and Devine (*Surg. Gynec. & Obst.* 105: 229, 1957) measured the end-expiratory carbon dioxide level of 100 routine recovery room patients and found that 25 per cent were ventilating inadequately. Hood *et al.* (*J. Thoracic Surg.* 36: 729, 1958), using respiratory volume and blood gas measurements, demonstrated that about 50 per cent of patients undergoing thoracic surgery had a significant depression of ventilation immediately after surgery. These findings caused us to re-evaluate the condition of recovery room patients in our institution; if respiratory depression was as prevalent as the previous studies suggested, it seemed likely that the somewhat empiric use of oxygen could accentuate the hypoventilation. Arterial blood pH, carbon dioxide tension and hemoglobin oxygen saturation were measured immediately after anesthesia and surgery in 23 patients breathing room air. No respiratory acidosis was found (mean pH 7.43, mean $P_{A_{CO_2}}$ 35.9). However, the arterial hemoglobin oxygen saturation was significantly depressed (93.8 per cent as compared to 97.1 per cent in a control group of 20 preoperative conscious patients).

In an attempt to identify the cause of this hypoxemia, 7 patients underwent "shunt studies" in which the amount of venous admixture was quantitated from blood oxygen data ob-

tained during 100 per cent oxygen breathing (to eliminate uneven ventilation effect). The preoperative "shunt" value was found to be 3.6 per cent; the postoperative "shunt" amounted to 10.8 per cent. In addition, the administration of nasal oxygen to 16 patients at a flow rate of 5 l./minute failed to increase the hemoglobin oxygen saturation significantly (mean saturation breathing room air, 92.7 per cent; mean saturation breathing nasal oxygen, 94.5 per cent). It seems likely that the shunt (not actually measured) in most of these patients must have exceeded 15 per cent, since this is the maximum degree of venous admixture which can be offset by 50 per cent oxygen (nasal oxygen). Uneven ventilation seems an unlikely explanation in view of the data of Brattstrom (*Acta chir. scandinav. (supp. 195) 1954*). These data suggest that subtle venous admixture may follow anesthesia and surgery and may represent a postoperative complication which is difficult to recognize by ordinary clinical methods. [Supported by research grant (H-1983C4), United States Public Health Service.]

Respiratory Obstruction in Normothermia and Hypothermia. HAROLD F. CHASE, M.D., DAVID J. LAFIA, M.D., AND MEARL A. KILMORE, B.S. *Departments of Anesthesiology and Neurosurgery, Jefferson Medical College, Philadelphia, Pennsylvania.* This report compares physiologic responses to respiratory obstruction during normothermia and hypothermia. Dogs were anesthetized with thiopental, their tracheas intubated, and then allowed to breath a mixture of nitrous oxide and oxygen. Arterial, inferior vena caval, external jugular, endotracheal and cisternal pressures, and the electrocardiogram were recorded on a Grass polygraph. Respiration was obstructed for ten minutes by forcing the animals to breath through a 15 gauge needle. Hypothermia of 30 C. was then produced by packing the dog in ice, and the respiratory obstruction repeated. Rectal temperature was recorded by a mercury thermometer. During normothermic obstruction there was an increase in all pressures, but the elevation in endotracheal pressure was proportionately larger. The electrocardiogram showed a sinus rhythm. There was a wide fluctuation of arterial, inferior vena