

hours, comparing treated groups with untreated surviving controls,  $K$  values were significantly lower in saline ( $P < 0.001$ ) and norepinephrine ( $P < 0.001$ ) groups, similar in the angiotensin group and significantly higher in the PLV-2 ( $P < 0.01$ ) group; the findings presumably reflecting the degree of sustained effects of early acute therapy on tissue RES activity. While these studies did not specifically differentiate the blood flow factor from RES tissue activity relative to phagocytic clearance measurements, this is not critical in regard to the predictive value of phagocytic indices since it is well established that hepatic blood flow and RES tissue activity both influence survival in the same direction. Furthermore the quantitative changes noted in the  $K$  values correlated closely with other critical parameters of shock; survival and microcirculatory vasomotor function studied under virtually identical experimental conditions (Altura and Hershey, *Amer. J. Surg.* 111: 186, 1966). RES function as measured quantitatively by phagocytic clearance of colloidal materials such as inert carbon in experimental intestinal ischemic shock is not only consistent with the biologic concept of the adaptive behavior of this homeostatic defense system but can possibly serve as a tissue level parameter of the course of the syndrome and its response to therapy. (Work supported by U.S.P.H.S. grant.)

**Human Lung Compliance During Prolonged Positive Pressure Ventilation.** BRIAN C. JUDD, M.D., and BENTON D. KING, M.D., *State University of New York at Buffalo, School of Medicine, Buffalo, New York.* It is generally agreed that positive pressure ventilation in anesthetized man causes a decrease in pulmonary compliance. However, it is not clear from studies to date how rapidly compliance falls and if it continues to fall when ventilation is continued for long periods. *Methods:* Lung compliance was measured in 16 patients undergoing operation involving the extremities or lower abdomen using halothane anesthesia. Strain gauges attached to an "Electronics for Medicine" recorder measured airway and esophageal pressure. Expired air was conducted through a pneumotachograph from a Sierra nonbreathing valve

and the resultant flow curve was electronically integrated to yield expired volume. End-expiratory  $\text{CO}_2$  was monitored in most of the patients with an infrared analyzer and was maintained at normal or near normal levels. After induction of anesthesia and endotracheal intubation, muscular relaxation was maintained with gallamine and ventilation was instituted with a Bird ventilator. A steady respiratory rate of 14-16/minute was maintained using a pressure limited cycle. The patient was then given 5-6 manual hyperinflations using a volume of at least 1,000 ml. and a pressure of at least 25 cm. of water. Ventilation was then returned to the previous pattern and compliance measured within one minute in 9 cases and within 2-3 minutes in the other 7. Ventilation was continued without change in ventilator settings for up to 3 hours and compliance measurements were repeated periodically. *Results:* (1) The compliance measurements made immediately after hyperinflation averaged 62.4 ml./cm. of water. (2) Compliance tended to decrease most rapidly in the first minute after hyperinflation. (3) After positive pressure ventilation for approximately 15 minutes, compliance was significantly decreased (29 per cent,  $P < 0.001$ ) when compared to values obtained immediately after hyperinflation. (4) Compliance showed no significant changes as pressure controlled ventilation was continued beyond 15 minutes for up to 3 hours without change in ventilator settings. (5) Initial compliance and later changes had no relationship to end-expiratory  $\text{P}_{\text{CO}_2}$ . *Discussion:* This work indicates that compliance does not change with pressure limited ventilation after the initial 10-15 minutes following hyperinflation. One of the clinical implications of this is that periodic hyperinflation, if it is to be effective in preventing decreased compliance, must be repeated at least every 10 minutes. However, the ideal frequency of hyperinflation cannot be stated from the results of this study alone. If compliance really shows a rapid decline immediately after hyperinflation, then the maneuver probably must be repeated at least once every minute or two if compliance is to be kept from falling. It was noted that compliance seemed to decrease very rapidly in the first minute after hyperinflation, but a greater

number of measurements must be obtained in this period to allow accurate statistical analysis. These observations may be interpreted as showing that some atelectasis may occur shortly after hyperinflation, but does not necessarily progress as ventilation is continued. It was noted that compliance during pressure controlled ventilation was at all times significantly lower than immediately after hyperinflation. This is in good agreement with other studies (Bendixen and others: *New Eng. J. Med.*, 269: 991, 1963). *Summary:* Lung compliance was measured in patients undergoing extremity and lower abdominal surgery during positive pressure ventilation using a pressure controlled cycle. Compliance decreased significantly in the first 10-15 minutes and remained stable thereafter. (This study was supported in part by a United States Public Health Service Training Grant (GM770).)

**A New Intravenous or Intramuscular Anesthetic.** C. HERSCHEL KING, M.D., and C. R. STEPHEN, M.D., *Division of Anesthesia, Duke University Medical Center, Durham, North Carolina.* New drugs which produce a state of analgesia or anesthesia continue to be evaluated because those available do not provide the attributes of an ideal drug. One such compound under study is C1-581, a derivative of phenacyclidine (Sernyl) (Domino, E. F., Chodoff, P., and Corssen, G.: *Clin. Pharmacol. Ther.* 6: 279, 1965). *Methods:* A total of 106 patients, ranging in age from 5 months to 68 years, received C1-581 either intramuscularly (38), intravenously (56), or by a combination of the two routes—an intramuscular dose followed by one or more intravenous injections (12). The lack of a suitable vein in awake infants was the principal indication for the intramuscular route. *Results:* An intravenous dose of 1 mg. per pound of body weight produced unconsciousness and surgical analgesia within 30 seconds, and adequate operating conditions lasted for 5 to 8 minutes. Further doses of 0.5 mg. per pound would restore the analgesic state for similar periods of time. With the onset of anesthesia, the eyes usually opened and the limbs became relaxed. However, pharyngeal and laryngeal reflexes remained active, and the upper res-

piratory airway remained patent, without benefit of manual support or the insertion of a mechanical airway. The pulse rate usually increased, the blood pressure rose (10 to 20 mm. of mercury systolic in children, 30 to 50 mm. of mercury in adults), and there was noticeable but not disturbing depression of the respiration for two or three minutes. During operation, random movements of the extremities were not uncommon, and athetoid or fibrillary-like motions of the mouth and tongue were frequent. To achieve surgical analgesia by the intramuscular route, injections of 4 to 5 mg. per pound were required. Surgical analgesia developed in 3 to 5 minutes and lasted for 20 to 30 minutes. In this series, 49 patients received doses of 1 to 2 mg. per pound, 36 were given 3 to 5 mg. per pound, and 20 had more than 5 mg. per pound. The recovery period following C1-581 was unlike that following other general anesthetics. Following intravenous administrations, verbal contact was established in 5 to 30 minutes, depending on the dose administered, whereas after intramuscular injections verbal contact was delayed for 35 to 150 minutes. Random movements and muscular rigidity were common, and when responding to stimuli patients had a faraway look in their eye and would state that "things looked and felt funny." About 50 per cent of the adults had definite hallucinations, often of a terrifying nature. Other complications were rare. No evidence of local irritation at the site of injection was found in any patient. Salivary secretions were enhanced unless atropine was given for premedication. No postoperative vomiting occurred. *Conclusions:* C1-581 confers potent analgesia with unconsciousness almost instantaneously, with minimal respiratory depression and a stimulant action on the cardiovascular system. The relatively slow recovery period, and the development of hallucinations in some adults, render the drug far from ideal, but do not detract from its potential value for certain diagnostic and therapeutic anesthetic procedures.

**Reversible Depression of Hippocampus by a Long-Term Microinjection of Dibucaine in Monkeys.** LUKE M. KITAHATA, M.D., and JOSÉ M. R. DELGADO, M.D., *Departments of*