Shanthaveerappa and Bourne, for it has not previously been described as investing the fasiculi so completely. *Conclusion:* Our results neither confirm nor deny that local anesthetic drugs diffuse across the dura directly into the cerebrospinal fluid. They do show that their distribution from the extradural space is complex, and that the sites of action are in the extradural and intradural roots, as well as in the neuraxis itself.

Phlebitis from Plastic Intravenous Catheters. FREDERICK W. CHENEY, JR., M.D., and JOHN R. LINCOLN, M.D., *Department of Anesthesiology, Maine Medical Center, Portland, Maine.* The incidence of significant phlebitis with the use of plastic intravenous catheters has been said to be about 16 per cent, with bacterial contamination suspect (Erwin, P.: Arch. Surg. *66:* 673, 1953). This study was initiated to determine the incidence and etiologic factors of this phenomenon. *Method:* Intracath (Bard 1514) catheters, 18 gauge, 8–12 inches in length, were inserted, usually in the basilic or cephalic veins of the arms, prior to the induction of anesthesia. The skin was prepared with aqueous Zephiran and the catheter inserted through a no. 14 needle. Three per cent achromycin ointment or a bland ointment was placed over the puncture site. This was covered with sterile gauze and taped securely. A record was kept of all solutions infused through each catheter, concomitant systemic antibiotic therapy, length of time the catheter was in place and the grade of reaction when removed. In addition, the terminal 3–5 inches of each catheter were cultured. All patients who showed no reaction at the time the catheter was removed were re-examined twenty-four hours later and any change in reaction noted. Reactions were classified as grade "A"—no reaction or slight erythema around the site of entrance of the catheter, or grade "B"—significant phlebitis associated with cellulitis, tenderness, or painful thrombosis of the vein. *Results:* Of the 137 cases studied, 60 had grade B reactions. The mean time the catheters were in place was 38.5 hours. A single application of achromycin ointment failed to reduce the incidence of phlebitis. The incidence of grade B reactions varied directly with the time the catheter was in place. The incidence of phlebitis increased from 9 per cent of those whose catheters were withdrawn in the 0–24 hour time period, to 58 per cent of those withdrawn in the 25–48 hour period, to 74 per cent of those withdrawn in the 49–72 hour period. Sixteen per cent of the patients had converted from grade A to B reactions when the twenty-four hour postwithdrawal visit was made. Patients who received heparin, 10 mg./1,000 ml. of infused solution, had their catheters in place significantly longer before the development of phlebitis than those who did not. The incidence of positive cultures was 9.5 per cent (13 of 137 cases) and most of these were staphylococci coagulase negative. There was no correlation of positive cultures with phlebitis. Acromycin ointment did not influence the incidence of positive cultures. No patient with a positive culture had any evidence of systemic symptoms. *Conclusion:* This study suggests that the major factor causing phlebitis and local tissue reactions from plastic intravenous catheters is mechanical rather than bacterial, and that adverse reactions are directly related to the length of time the catheter is in place. No other factor studied seemed to have any influence on the incidence of phlebitis, except heparin, which increases the length of time a catheter may be kept in place without phlebitis.

Evaluation of Halothane Toxicity by Tissue-Culture Methods Halothane. GUENTER CORSSEN, M.D., and ROBERT B. SWEET, M.D., *Department of Anesthesiology, The University of Michigan Medical School, Ann Arbor, Michigan.* Clinical studies of anesthetic agents can hardly be relied on to furnish objective evidence of drug toxicity because of the difficulty of evaluating biochemical reactions as well as the impossibility of setting up strict controls. The experimental techniques involved in tissue-culture methods appear to offer a much more efficient means of analyzing the effects of drugs. Recently, such methods were used in a study of the possible cytotoxic effects of halothane, and preliminary results indicated that cultured human liver cells may be affected adversely by this agent. *Method:* In this study, human liver cells under culture

were transferred to perfusion chambers filled with nutrient medium (basal Eagle and 20 per cent human serum). When unimpaired growth of the cells had been established, the control medium was replaced by medium containing halothane, 0.3 ml. of halothane per 100 ml. of medium. With the aid of phase-contrast microphotography and time-lapse microcinematography certain morphologic changes such as contraction and shrinkage of cells could be recorded within 12 hours after perfusion had begun. Fat droplets occasionally appeared in the cytoplasm. As a result of these changes, cytoplasmic activity was increasingly depressed and outgrowth of the epithelial sheet inhibited. Only a few of the cultured cells remained intact after three days of exposure to halothane. A significant problem was the low solubility of halothane in water, which necessitated vigorous shaking of the halothane-balanced salt-serum solution for up to 6 hours, to insure complete dispersion of the halothane. About 24 hours after halothane was added to the medium, a precipitate was formed which has not been identified but which may have indirectly contributed to the cytologic changes, by altering the chemical composition of the nutrient medium. Further investigation is needed to clarify this point. *Conclusions:* Plans for future studies include perfusion experiments using weaker halothane concentrations and identical experiments with other fluorinated hydrocarbons such as chloroform and methoxyflurane. Results of such studies must be compared with those reported here, before conclusions can be drawn regarding hepatic toxicity of halogenated anesthetic compounds. It appears, however, that tissue-culture studies of liver cells may constitute a valuable tool for objectively measuring the possible adverse effects of halothane and related compounds.

Accuracy of Manual Ventilation: Comparison of Closed and Semiclosed Breathing Systems. L. D. EGBERT, M.D., and M. B. LAVER, M.D., *Anaesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, Boston, Massachusetts.* Compliance of the lungs and thorax change frequently during anesthesia. The skillful anesthetist feels this as a change in resistance when he squeezes the anesthesia balloon. If the lungs become stiffer, he applies greater pressure in order to maintain a normal tidal volume, and normal gas exchange in the lungs. *Method:* We examined the degree of skill in recognizing compliance changes in 22 fully trained physician anesthetists by having them control the respiration of a set of bellows (Drager training thorax supplied by Air Products Medical Division). Pressure was measured with a strain gauge transducer and volume with a pneumotachograph. Without the anesthetist being aware of it, we changed the compliance of the bellows; a screen prevented him from watching. He was asked to note any changes in stiffness of "his patient's lungs." He was employed also at reading a book (simulating taking of blood pressure, etc.). Each subject was told to keep the volume and rate of respiration constant, altering as necessary the pressure which he applied to the anesthesia balloon. He was allowed to adjust the volume of gas in the balloon as desired. *Results:* While watching the "lung," each of the anesthetists was able to keep tidal volume almost constant. Also, each anesthetist kept tidal volume near constant when the screen blocked his view as long as compliance remained constant. When compliance was lowered (from 30 ml./cm. of water to as low as 15 ml./cm. of water), the anesthetists raised the pressure to ventilate the bellows. However, the pressure rise was insufficient to maintain the control tidal volume. Eleven of the subjects allowed tidal volume to fall to less than 50 per cent of what they thought they were ventilating. We found greater error with the semiclosed system than with the closed system. The average control tidal volume was 350 ml. (compliance 30 ml./cm. of water). With compliance at 15 ml./cm. of water, the average tidal volume fell to 215 ml. with the semiclosed system and only to 275 ml. with the closed system ($P < 0.05$). The anesthetists made more correct statements about the "patient's" condition while using the closed system; they noticed leaks in the system more rapidly using the closed system than the semiclosed. We have found differences between individuals related to the length of time in clinical practice. We found also that the average error of the anesthetists associated