thesia. In those subjects in whom the ether concentration was decreased or discontinued, the electroencephalogram returned to the pre-ether pattern in the reverse of the previous order. Extensive psychological testing in some intelligent subjects indicated that changes were not marked until the 3 per cent ether level had been maintained. However, at this point there was usually euphoria, inability to learn non-meaningful material, and decline in memory for rote and meaningful material. Capacity for abstraction did not seem to be particularly impaired. Subsequent testing on another day indicated considerable amnesia for much of the ether test period. By this technique of ether administration it was impossible to produce analgesia of sufficient intensity at the 3 per cent level to have permitted a skin incision to be made. This concentration of ether is considerably higher than the mean concentration of 1.2 per cent reported during ether analgesia by Ebersole and Artusio (*Anesthesiology 19: 607, 1958*). In this study testing for analgesia was performed before surgical anesthesia was ever attained whereas Artusio (*J. Pharmacol. & Exper. Therap. 111: 343, 1954*) first produced surgical anesthesia before subsequently utilizing analgesia.

Clinical Investigation of R01-5733, a New Curare Antagonist. LUDWIG R. KOUKAL, M.D., FRANCIS F. FOLDES, M.D., JOHN F. ZEEDICK, M.D., AND DERYCK DUNCALF, M.D. *Department of Anesthesiology, Mercy Hospital and Section on Anesthesiology, Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, Pa.* Investigation of the structure-action relationship of neostigmine analogs (*Foldes et al., J. Pharm. & Exper. Ther. 122: 457, 1958*) prompted the synthesis of a new cholinesterase inhibitor, R01-5733 (2-hydroxybenzyl trimethylammonium bromide dimethyl carbamate). In *in vitro* laboratory studies, it was found to be twice as potent an inhibitor of human plasma and red cell cholinesterase as neostigmine. According to L. O. Randall (*personal communication*) it was slightly less toxic in mice on oral administration, and on intravenous administration slightly more toxic than neostigmine; in cats its effect on neuromuscular transmission was greater than that of neostigmine. In the present study R01-5733 was administered to two groups of human subjects. Ten subjects of the first group were lightly anesthetized with a previously described technique (*Rendell-Baker et al., Brit. J. Anaesth. 29: 304, 1957*). After stabilization of the level of anesthesia at 0 time, 1.0 mg./kg. gallamine, and 5 minutes later 0.01 mg./kg. R01-5733 was injected intravenously. Respiratory rate, tidal and minute volumes, pulse rate and blood pressure were determined before and at 3, 8, 12, 16 and 20 minutes after the injection of gallamine. There was no significant change in respiratory rate throughout the observation period. The average respiratory tidal and minute volumes decreased to less than 50 per cent of the control values 3 minutes after the administration of gallamine but returned to and stayed above control value within 3 minutes following the injection of R01-5733. As noted previously (*Foldes et al., Anesth. & Analg. 33: 122, 1954*), pulse rate and to a lesser extent systolic blood pressure increased after gallamine, but gradually returned to control values within 15 minutes after the administration of R01-5733. In a second group of 50 patients, in whom muscular relaxation for intra-abdominal surgery was produced by gallamine or *d*-tubocurarine, respiratory tidal volume, pulse rate and blood pressure were determined at the end of surgery before and after the intravenous administration of 0.01 mg./kg. R01-5733. The average tidal volume of this group increased from 118 ml. to 371 ml. within 3 minutes after the administration of R01-5733. No change in pulse rate or blood pressure was observed. Recurarization was not observed in any of the patients studied. Although no additional parasympatolytic agent was used with R01-5733, the only indication of any muscarinic effect was increased salivation in about one half of the cases. Because R01-5733 can be safely administered in doses necessary for the correction of residual neuromuscular block at the termination of surgery without additional atropine, it is the agent of choice of the presently available curare antagonists. R01-5733 was also administered both intravenously and by mouth to a group of myasthenic patients. In these patients, however, R01-5733 did not seem to offer any advantages over other anticholinesterases in clinical use.