

This Week's Citation Classic™

Virtue R W, Alanis J M, Mori M, Lafargue R T, Vogel J H K & Metcalf D R. An anesthetic agent: 2-ortho-chlorophenyl, 2-methylamino cyclohexanone HCl (CI-581). *Anesthesiology* 28:823-33, 1967.
[Div. Anesthesiology, Cardiovascular Pulmonary Lab., and Electroencephalography Lab., Univ. Colorado Medical Ctr., Denver, CO]

Animal experiments indicated that CI-581 anesthesia does not sensitize a heart to epinephrine, and that it does not depress spontaneous respiration, while giving excellent analgesia. Human beings responded similarly in a variety of surgical circumstances. The drug failed to depress reflexes and afforded no relaxation. [The SC¹® indicates that this paper has been cited in over 150 publications since 1967.]

Robert W. Virtue
Department of Anesthesiology
University of Colorado Medical Center
Denver, CO 80262

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"Anesthesiologists are constantly looking for better and safer agents. When information came from the University of Michigan that a congener of Sernyl (Sernyl produced analgesia but was followed by extreme mental disturbance and excitement) appeared which had fewer undesirable qualities, it seemed valuable to observe firsthand what the drug would do. Gracious cooperation by Corsen, Domino, and McCarthy,^{1,3} as well as support from the Parke Davis Co., led to observation in Ann Arbor of the effects of the drug on patients undergoing eye surgery. Recovery after use of the new congener (ketamine) was substantially different from that after the common anesthetics then in use. The drug did not depress respiration as other agents (except ether) did. It is the only anesthetic agent that can be intravenously administered that permits adequate spontaneous respiration. After preliminary animal experiments at the University of Colorado, the drug was given to several surgical patients in unusual circumstances, such as a man who was to have an anterior neck fixation because of a dislocation of vertebrae. It

was deemed dangerous to move the neck (the patient was immobilized with tongs). Because of the impossibility of holding a mask while the surgeon operated, and the difficulty of inserting an endotracheal tube without moving the neck, normal anesthetic procedures were ruled out. With ketamine there was no problem because spontaneous respiration could continue. Our work extended the use of ketamine to various types of surgery and indicated that, when one realized the limitations of ketamine, it could be the safest agent available.

"Approximately ten percent of patients have vivid dreams during anesthesia with ketamine. Some are disagreeable, but not all. One woman, after three previous anesthetics, said, 'Everyone should have that anesthetic; it was so wonderful!' Analysis by Albin *et al.*⁴ of the mental state of persons who had received ketamine showed that, compared to those who had other agents, dreams were not excessive.

"Due to commercial manipulations, distribution of ketamine was allocated to a second drug outlet, which in its effort to get the drug on the market quickly, sent samples to many anesthesiologists around the country without stressing the precautions necessary for its proper use. The drug soon came into disfavor because warnings that recovery needed a quiet environment (the drug gives no relaxation) and that the patient should be undisturbed during recovery were not given. Some years elapsed, therefore, before the drug could find its proper place in anesthesiology.

"After about 15 years, the position of ketamine in anesthesiology has been reasonably stabilized, as indicated in a 1982 review of its properties and uses.⁵

"Citations to the investigations of ketamine are probably due to the observations made at the University of Colorado which were the first to include its use in a variety of human surgical cases, and which provided EEG data along with usual physiological studies."

1. McCarthy D A, Chen G, Kaump D H & Ensor C. General anesthetic and other pharmacological properties of 2-(o-chlor-phenyl)-2-methylamino cyclohexanone HCl (CI-581). *J. New Drugs* 5:21-33, 1965.
2. Domino E F, Chodoff P & Corsen G. Pharmacologic effects of CI-581, a new dissociative anesthetic, in man. *Clin. Pharmacol. Ther.* 6:279-91, 1965.
3. Domino E F. Citation Classic. Commentary on *Clin. Pharmacol. Ther.* 6:279-91, 1965. *Current Contents/Life Sciences* 27(25):16, 18 June 1984.
4. Albin M, Dresner J, Paolino A, Sweet R, Virtue R & Miller G. Long term personality evaluation in patients subjected to ketamine hydrochloride and other anesthetic agents. (Abstract.) (American Society of Anesthesiologists) *Abstracts of scientific papers, 1970 ASA annual meeting.* Park Ridge, IL: ASA, 1970, p. 166-7.
5. White P F, Way W L & Trevor A J. Ketamine—its pharmacology and therapeutic use. *Anesthesiology* 56:119-36, 1982.