

Effects of Propranolol on Epinephrine-induced Arrhythmias during Halothane Anesthesia in Man and Cats. ETSUTARO IZENO, M.D., KATSUHISA YASUDA, M.D., and YOSHIO HATTORI, M.D., *Department of Anesthesia, School of Medicine, Tokyo Medical and Dental University, 1-5-47, Yushima, Bunkyo-Ku, Tokyo, Japan.* The successful treatment of ventricular arrhythmias with propranolol during anesthesia has been reported. The injection of epinephrine in man and animals may elicit cardiac arrhythmias in the presence of halothane. This study was done to determine the effects of propranolol in preventing cardiac arrhythmias which might occur when epinephrine is used during halothane anesthesia in man and cats. *Method: Clinical Cases:* The ECG was monitored during halothane anesthesia in 120 E.N.T. cases in which epinephrine was locally injected or topically applied to nasopharyngeal mucosa for hemostasis. Respiration was assisted to maintain end-tidal CO_2 at 4-5 per cent throughout the operation. The patients were classified in two groups. Group A: 50 $\mu\text{g}/\text{kg}$. of propranolol was given prophylactically to 52 patients in whom epinephrine was injected (0.15-4.6 $\mu\text{g}/\text{kg}/\text{hr}$.) or topically applied (35.7-1,254.8 $\mu\text{g}/\text{kg}/\text{hr}$.) Group B: No propranolol was used in 62 patients in whom epinephrine was injected (0.54-10.7 $\mu\text{g}/\text{kg}/\text{hr}$.) or topically applied (15.0-279.0 $\mu\text{g}/\text{kg}/\text{hr}$.) during halothane anesthesia. *Results:* In Group A no ventricular arrhythmias were observed even though excessive amounts of epinephrine were used. In Group B 13 patients developed ventricular arrhythmias during halothane anesthesia. These arrhythmias were controlled easily by injection of 50 $\mu\text{g}/\text{kg}$. of propranolol. There were no complications which can be attributed to propranolol. *Animal Experiments: method:* In 35 cats anesthesia was induced and maintained with 1 per cent halothane in oxygen. End-tidal CO_2 was measured by Capnograph. The animals were divided into two groups. In group A, ventilation was adjusted to maintain 4-5 per cent of end-tidal CO_2 , and a dose of epinephrine which would produce ventricular arrhythmias up to at least 10 P.V.C. in one minute was determined. Fifty $\mu\text{g}/\text{kg}$. of propranolol was given and

changes in the arrhythmic doses of epinephrine were measured. In group B CO_2 was administered to elevate end-tidal CO_2 to 8 per cent, an arrhythmic dose of epinephrine was determined, and the effects of propranolol were studied using the same technique as in group A. *Results:* In group A the arrhythmic dose of epinephrine was found to be 5.9 $\mu\text{g}/\text{kg}$. This increased to 21 $\mu\text{g}/\text{kg}$. after the administration of propranolol. In group B half of the animals developed P.V.C. without injection of epinephrine. The arrhythmic dose in this group was 0.68 $\mu\text{g}/\text{kg}$. It increased to 3.75 $\mu\text{g}/\text{kg}$. after the use of propranolol. *Summary:* In 52 patients, receiving 50 $\mu\text{g}/\text{kg}$. of propranolol no ventricular arrhythmias occurred during halothane anesthesia with epinephrine injections. Without the prophylactic use of propranolol, epinephrine produced ventricular arrhythmias in 13 of 68 patients during halothane anesthesia. These were abolished by using 50 $\mu\text{g}/\text{kg}$. of propranolol. In animal experiments the average arrhythmic dosage of epinephrine during halothane anesthesia was increased 3.5-5.5 times over control values after the injection of propranolol. *Conclusions:* The results of this study appear to justify the use of propranolol for both prophylaxis and treatment of epinephrine-induced arrhythmias during halothane anesthesia.

The Use of In-vitro Technique in the Development of New Neuromuscular Blocking Agents. JOANNES H. KARIS, M.D., RICHARD J. KITZ, M.D., and WILLIAM L. NASTUK, PH.D., *Departments of Anesthesiology and Physiology, College of Physicians and Surgeons, Columbia University, New York, N. Y.* Many currently-used neuromuscular blocking agents produce blocks which endure longer than required, and many have unwanted side effects. A drug that produces a nondepolarizing block of short duration is clearly desirable. Several series of new quaternary ammonium esters which can be hydrolyzed by acetylcholinesterase and/or plasma cholinesterase, recently synthesized by Drs. Kitz and Ginsburg, may have short durations of activity *in vivo*. To evaluate these agents, we chose an *in vitro* technique to collect specific information about potency as well as mode of