information is available on the effects of narcotic antagonists on narcotic induced circulatory depression in man. This study was undertaken to determine whether protection against such circulatory depression was afforded by the narcotic antagonists. Control observations of pulse rate, blood pressure, respiratory rate, and electrocardiographic tracings were made in both the horizontal and 25 degree head-up position in 40 healthy adult males and females between the ages of 18 and 58. These subjects received no medication prior to their arrival in the operating room. At the start of the test period, 20 subjects each received 1.5 mg./kg. meperidine, and 20 others 0.6 mg./kg. alphaprodine intravenously. Half the subjects in each group received 0.02 mg./kg. levallorphan tartrate intravenously two minutes prior to the injection of the narcotic. The observations made during the control periods were repeated at 2, 4, 6, 9, 12, and 15 minutes. At 16 minutes, the subjects were placed in the 25-degree head-up position, and the observations were repeated at 18, 21, 24, 27 and 30 minutes. No significant changes in pulse rate and blood pressure were observed after the use of alphaprodine alone or preceded by levallorphan either in the horizontal or the head-up tilt position. Alphaprodine alone caused a significant decrease in the respiratory rate. This was prevented by the prior administration of levallorphan. No remarkable changes were seen in the electrocardiographic tracings. In contrast, the intravenous administration of meperidine caused a moderate rise in pulse rate and fall in blood pressure in the horizontal and a statistically significant fall of pressure in the head-up tilt position. The circulatory effects were only partially prevented by the antagonist. In three subjects, who received meperidine alone and in one who also received levallorphan, the experiment had to be discontinued 3 to 6 minutes after the subjects were placed in the head-up tilt position because of severe hypotension. Meperidine alone or after levallorphan caused no significant change in the respiratory rate or electrocardiographic tracings. The findings presented indicate that narcotic antagonists do not afford protection against the primarily peripheral effects of meperidine.

Incidence of Cardiac Arrhythmias During Anesthesia. WILLIAM A. SIMS, M.D., DAVID J. BONE, M.D., AND ROBERT B. DODD, M.D. *Department of Anesthesiology, Barnes Hospital, Washington University School of Medicine, St. Louis, Missouri.* The incidence of cardiac arrhythmia has been studied in 364 unselected surgical patients by means of continuous electrocardiographic monitoring utilizing wall-mounted oscilloscopes. The age range of the patients in this series was from 2 to 96 years with a mean age of 52 years and a median of 54 years. This group thus exceeded the mean age of the general surgical population by seventeen years. There was no selection as to type of anesthetic agent or technique used, but over half (192) of the patients received ether as the primary anesthetic agent. The bulk of the anesthesias were administered by anesthesiology residents and nurse anesthesia students. Arrhythmias reported by the nurses were confirmed by a staff anesthesiologist. Since monitoring was done by visualization of oscillographic tracings and permanent records were rarely made, reporting of transient tachycardias and bradycardias was unsatisfactory. Two cardiac arrests occurred during the series. Both were standstills and were successfully resuscitated; one by thoracotomy and artificial circulation, the other by vigorous washing out of the anesthetic mixture with 100 per cent oxygen. The results of the study to this time show: (1) Cardiac arrhythmia of some type occurred in 32.9 per cent of the patients subjected to anesthesia and surgery. The actual incidence may be somewhat higher since one-third of the cases were anesthetized by nurse students who recognized arrhythmias half as frequently as the anesthesia residents. (2) Arrhythmias occur with increasing frequency with increasing age. The average age of patients exhibiting arrhythmia was 55.8 years. For patients not showing arrhythmia it was 47 years. The incidence of arrhythmias in patients over the age of 50 years was significantly greater than in those under 50 years ($p < .005$). (3) There is a much higher incidence of arrhythmias, 59.5 per cent, in patients having evidence of pre-existing cardiac disease than in patients having negative cardiac history and findings, 25 per cent. (4) The most frequent arrhythmia noted was A-V dis-

sociation. It occurred in 12.5 per cent of the cases and comprised 50 per cent of the arrhythmias diagnosed. It was associated with hypoxia, surgical manipulation or deepening of anesthesia. Premature ventricular contractions occurred in 4 per cent of the cases and made up 40 per cent of the recognized arrhythmias. Other arrhythmias noted in the series were auricular premature contractions, auricular fibrillation, A-V block, and bundle branch block. (5) The incidence of arrhythmia was not affected by the belladonna alkaloid used in premedication, sex of the patient, or type of inhalation agent used. (6) Constant electrocardiographic monitoring of patients under anesthesia has proven to be a valuable adjunct to the administration and supervision of clinical anesthesia.

Studies of Narcotic Antagonists as Analgesics. JANE TELFORD, M.D., YOSHIO KUROSU, M.D., AND ARTHUR S. KEATS, M.D. *Division of Anesthesiology, Baylor University College of Medicine, Houston, Texas.* The previous demonstration that nalorphine was a potent analgesic in man led us to the investigation of other narcotic antagonists as analgesics in the search for a potent analgesic without undesirable side effects. Recently we have studied in man two morphinan derivatives reported to antagonize morphine in animals. These are (−) 3-hydroxy-N-(3,3, dimethylallyl)-morphinan hydrobromide (NIH 7446 and (−) 3 hydroxy-N-propargyl morphinan tartrate (NIH 6045). Initially analgesic potency of these drugs was determined. On a milligram basis NIH 7446 was equally, and NIH 6045 was twice as potent as morphine as an analgesic in relieving postoperative pain. However, when given in equivalent analgesic doses to normal subjects, NIH 7446 was only half as potent and NIH 6045 equally as potent as morphine in depressing respiration. To estimate the potency of these drugs as morphine antagonists, anesthetized patients were used. Patients under light thiopental-nitrous oxide-oxygen anesthesia were given morphine or a morphine antagonist intravenously to a total dose averaging 1 mg./kg. Controlled respiration was maintained throughout the operation with succinylcholine by infusion when necessary. After operation, alveolar ventilation and alveolar P_{CO_2} were measured simultaneously. After a suitable control period, one of the following was given intravenously: placebo, nalorphine 2.5 mg., NIH 7446 2.5 mg., or NIH 6045 2.5 mg. Measurements were repeated at 5 and 10 minutes after drug administration. Nalorphine in doses of 1 mg., 2.5 mg., and 5 mg. dramatically antagonized the respiratory depression of morphine (1 mg./kg.). In 3 patients who had received morphine 1 mg./kg., NIH 7446 produced little antagonism. In an additional 3 patients, the respiratory depression of 1 mg./kg. of NIH 7446 was similar in degree to that of morphine and was dramatically antagonized by nalorphine. NIH 6045 in doses of 2.5 mg. antagonized morphine induced respiratory depression in a manner similar to that of nalorphine. However, when NIH 6045 was given to 5 patients in doses of 1 mg./kg. intravenously, it produced only half the respiratory depression of morphine and only one quarter of that anticipated from studies of respiratory depression in normal subjects. When 2.5 mg. of nalorphine was given after NIH 6045, there was no significant change in respiration. Similarly nalorphine in doses of 10 mg./70 kg. depressed the respiration of normal subjects but in doses of 1 mg./kg. intravenously produced little respiratory depression in anesthetized patients. NIH 6045 appears to act like nalorphine, whereas NIH 7446 appears to be a morphine-like drug. The quantitative discrepancy between the respiratory depression in normal subjects following a small dose of NIH 6045 and a large dose in anesthetized patients suggests that the drug may have a dual action which depends on dosage.

Studies on the Effect of Urea on Blood Pressure and Volume. JOHN TENCH, M.D., MANUCHER JAVID, M.D., AND DAVID GILBOE, PH.D. *Departments of Anesthesiology and Neurosurgery, University of Wisconsin Medical School, Madison, Wisconsin.* Analysis of over 200 anesthetic charts of patients who received urea during craniotomy revealed a consistent pattern of blood pressure increase averaging 26 mm. Hg above stabilized blood pressure. This was later followed by a decrease to an average of 20 mm. Hg below stabilized blood pressure when adequate blood replacement was not initiated. Preliminary studies under-