

An electronic difficulty, ECG pick-up interference, was encountered early in the investigation. The QRS causes an imperceptible disturbance presumably because frequencies dominant in the QRS are efficiently rejected by the flowmeter. The P wave is the major source of disturbance which is of random phase and polarity from beat to beat. Its magnitude was reduced by retracting the atrial appendage, and by placing a 1 cm. \times 1 cm. piece of tinfoil between the artery and the underlying myocardium. (This makes it more likely that the ECG will affect both electrodes equally and so be cancelled out.) The arterial pressure was monitored simultaneously from the femoral artery using a Statham gauge transducer. Lead 2 of the electrocardiogram was monitored continuously. *Results:* The normal pattern of coronary blood flow did not deviate grossly from that reported by Gregg and Green (Gregg, D. E.: *Coronary Circulation in Health and Disease*. Phila., Lea & Febiger, 1950) with the differential pressure flowmeter. The effect on coronary arterial flow from momentary occlusion of the coronary artery was studied. After a fall of arterial flow to zero, a measurable reactive hyperemia regularly occurred. The normal physiological relation of systemic arterial pressure to coronary flow was demonstrated. Also, there was noted an increase in coronary flow with increases in heart rate up to 150 beats per minute but a decrease with further increases in heart rate. *Conclusion:* A series of observations are planned on alterations in mean coronary arterial flow and pulsatile characteristics produced by the administration of drugs and various situations encountered during anesthetic practice. The results should be of value to the anesthesiologist in the anesthetic management of the patient with coronary artery disease.

Effects of N-Allyloxymorphone-Narcotic Mixtures in Anesthetized Subjects. G. M. DAVIDSON, M.B., F. F. FOLDES, M.D., D. DUNCALF, M.D., E. S. SIKER, M.D., and S. KUWABARA, M.D., *Departments of Anesthesiology, Mercy Hospital and the University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.* (Dr. Folds' present address: Montefiore Hospital, New York.) *Method:*

Sixty subjects, given premedication of 100 mg. pentobarbital and 0.3 to 0.4 mg. scopolamine hydrobromide, were lightly anesthetized with thiopental sodium and nitrous oxide-oxygen. Control values of respiratory rate, tidal and minute volumes and of pulse rate and blood pressure were recorded after induction of anesthesia. The 60 subjects were divided into six groups of ten. The following drugs were administered intravenously over a 30-second period to the members of the groups: group I, 0.02 mg./kg. oxymorphone hydrochloride; group II, 0.02 mg./kg. oxymorphone plus 5 μ g./kg. N-allyloxymorphone hydrochloride; group III, 0.2 mg./kg. morphine sulphate; group IV, 0.2 mg./kg. morphine plus 5 μ g./kg. N-allyloxymorphone; group V, 2.0 mg./kg. meperidine hydrochloride; group VI, 2.0 mg./kg. meperidine plus 5 μ g./kg. N-allyloxymorphone. *Results:* When administered alone, the three narcotics caused marked respiratory depression. The respiratory rate and minute volume decreased to about 25, 55, and 70 per cent of control after meperidine, oxymorphone and morphine, respectively. When administered together with 5 μ g./kg. N-allyloxymorphone, the respiratory rate and minute volume decreased only to about 75, 85 and 90 per cent of control with meperidine, oxymorphone and morphine, respectively. These doses of narcotics caused a 10 to 20 per cent decrease of pulse rate and systolic and diastolic blood pressure. These circulatory effects were not significantly affected by the simultaneous administration of N-allyloxymorphone. Judging from the reaction to the skin incision made 12 to 15 minutes after the administration of the narcotics or the narcotic-N-allyloxymorphone mixtures and from the mg./kg./minute thiopental doses, the admixture of N-allyloxymorphone caused no significant decrease in the analgesic potency of the narcotics. In ten other subjects, who, in addition to pentobarbital and scopolamine, also received 50 to 100 mg. meperidine in their premedication, the apparent protective effect of the admixture of 5 μ g./kg. N-allyloxymorphone to 0.02 mg./kg. oxymorphone was greater than in the subjects of group II not premedicated with a narcotic. *Conclusion:* Our findings indicate that although for the supplementation of anesthesia, the analgesic effect of 2.0 mg./kg.

meperidine, 0.2 mg./kg. morphine and 0.02 mg./kg. oxymorphone are about the same, meperidine causes considerably more, and morphine considerably less, respiratory depression than oxymorphone. The results of this study confirmed the previously reported (Lunn, J. N., and others: *Pharmacologist* 3: 66, 1961) findings on the protective and antagonistic effects of N-allyloxymorphone on narcotic-induced respiratory depression.

Halothane Uptake by Man at a Constant Alveolar Concentration. EDMOND I. EGER, II, M.D., and NERI P. GUADAGNI, M.D., *Department of Anesthesia, University of California Medical Center, San Francisco, California.* **Method:** Halothane uptake by man at a constant alveolar concentration was determined in ten healthy human beings. Uptake was obtained from the difference between inspired and expired (end-tidal) concentrations times alveolar minute volume. The technique and instruments used are essentially the same as those of Sechzer, Linde, and Dripps (*ANESTHESIOLOGY* 23: 161, 1962), except that in our study the inspired concentration of halothane was periodically altered to hold the end-tidal concentration constant. Figures thereby obtained were converted to milliliters uptake per 70 kg. at an alveolar concentration of 0.8 per cent halothane. **Results:** Uptake during the first minute averaged 81 ml.; was 47 ml. at five minutes, 34 ml. at ten minutes, and 28 ml. at 20 minutes. Uptake decreased slowly thereafter and at 160 minutes was 12 ml./minute. Considerable variation in uptake occurred; the mean standard deviation equalled one-third of the uptake figure. **Discussion:** If alveolar anesthetic concentration equals brain concentration, a constant alveolar concentration reflects a relatively constant "depth" of anesthesia. The above figures thus provide a guide to the average amount of halothane required to maintain a stable light level. Deeper anesthesia would require somewhat greater quantities. An increase in alveolar concentration would not result in a proportional increase in uptake because of the concomitant decrease in cardiac output. [Supported in part by United States Public Health Service Grant GM-K3-17, 685, and 2G-63.]

Determination of Anesthetic Potency.

ROBERT M. EPSTEIN, M.D., S. H. NGAI, M.D., DONALD C. BRODY, M.D., and DAVID M. RITTENBERG, Ph.D., *Departments of Anesthesiology, Pharmacology, and Biochemistry, Columbia University, College of Physicians and Surgeons, New York, New York.* Recent proposals of a new theory of the mechanism of the anesthetic action of inert gaseous agents depend on correlation of certain physical properties of these agents with the partial pressures required to produce anesthesia. These pressures, from the literature, are useful approximations based on observation of small numbers of animals, differing in species and studied by varying techniques. One way to test theories of anesthetic action would be to detect small shifts in anesthetic potency after maneuvers which may alter the affinity of these agents for lipid or watery phases in the brain. To make such testing feasible, a more precise measurement of the absolute potency of anesthetics and the range of variation encountered is necessary. **Method:** The median anesthetic dose (AD_{50}) of a number of commonly employed agents was determined in Swiss mice, using the loss of righting reflex as an end point. Approximately ten mice per dose were exposed in a plastic chamber to a high flow of anesthetic in oxygen at constant inspiratory concentrations. The period of exposure was sufficiently long to allow brain equilibration to occur. Concentrations of the anesthetics were determined by techniques appropriate to the individual agents. **Results:** The AD_{50} and 95 per cent confidence limits as gas tensions in millimeters of mercury determined by probit analysis were: chloroform 6.4 (6.0-6.8), halothane 12.9 (12.6-13.2), cyclopropane 125 (121-129), ethylene 1,033 (1,003-1,081), and nitrous oxide 1,144 (1,112-1,179). Reproducibility was tested by repetition of studies for nitrous oxide. The separately determined values were 1,135 and 1,152 mm. of mercury and were not significantly different. Nitrous oxide was, therefore, used for further studies. Pretreatment of mice with 0.9 per cent NaCl in large doses (60 ml./kg. subcutaneously 48 and again 24 hours before study) increased the N_2O AD_{50} to 1,265 (1,238-1,297, $P < .05$), with reproducibility similar to that found in the controls. Pretreatment with 0.9 per