per cent, respectively. *Summary:* These findings suggest that prophylactic digitalization improves the inotropic state of the normal heart, especially the ability to develop the maximum force, during anesthesia. (Supported by USPHS Grant HE-01711 from the National Heart Institute.)

Effects of Halothane on Mitochondrial Oxygen Uptake: Site of Action. P. J. COHEN, M.D., B. E. MARSHALL, M.D., and J. LECKY, B.A., *Department of Anesthesia, University of Pennsylvania School of Medicine, Philadelphia, Penna.* *Methods:* Rat liver mitochondria were exposed for 20 minutes to halothane vaporized in air. Control mitochondria were treated similarly but exposed to air alone. In order to study reversibility, a portion of the exposed suspension was then equilibrated with air for an additional 20 minutes. Oxygen uptake was measured polarographically. Substrate (glutamate, 10 mM; succinate, 10 mM; and dihydronicotinamide adenine dinucleotide [NADH], 280 μM), inorganic phosphate, 10 mM; oxygen, air-saturated reaction medium; and adenosinediphosphate, 250 μM, were not rate-limiting. Since NADH does not penetrate intact mitochondria, the mitochondrial suspension was further treated by aging and resuspension in distilled water when NADH was to be substrate. *Results:* When *glutamate* was substrate, halothane produced a dose-related decrease in oxygen uptake. Halothane (0–10 per cent) had no effect on oxygen uptake when *succinate* was substrate. The effect of halothane on *NADH* oxidation was similar to that observed when *glutamate* was oxidized. In both cases inhibition was dose-related, was observed when less than 1 per cent halothane was administered, and was completely reversible provided that less than 3 per cent halothane had been used. Maximum inhibition (oxygen uptake 25 per cent of normal) was seen following exposure to 4 per cent halothane; concentrations greater than this had no additional effect. The addition of 5 mM amytal permitted the evaluation of amytal-sensitive oxygen uptake during *NADH* oxidation (Exper. Cell. Res., Suppl. 3, 124, 1955). Addition of amytal to control mitochondria reduced oxygen uptake to 25 per cent of normal; this represents amytal-insensitive respiration. In mitochondria exposed to less than 4 per cent halothane, amytal resulted in a further diminution of respiration to 25 per cent of control. In mitochondria whose oxygen uptake had already been reduced to 25 per cent of normal by concentrations of halothane greater than 4 per cent, amytal produced no further changes. Similar findings were made when amytal was added to a suspension oxidizing *glutamate*. *Summary:* The action of halothane upon the mitochondrial respiration chain is to inhibit NADH oxidation reversibly. Furthermore, since halothane inhibits only amytal-sensitive respiration, total oxygen uptake is not reduced below 25 per cent of normal by even high concentrations of halothane. (Supported in part by USPHS Grants GM-5-P01-09970-05, 5-T1-GM-215-01, 1-P01-GM-15430-01, and a grant from the Wellcome Trust.)

A Graphic Analysis of Cardiopulmonary Changes Following Major Surgery. F. J. COLGAN, M.D., and P. D. MAHONEY, M.D., *University of Rochester School of Medicine and Dentistry, Rochester, N. Y.* *Methods:* Twelve patients were studied before and after major upper abdominal surgery to determine the significance of any changes in cardiac output and FRC on intrapulmonary shunting. From this study, a method for the sequential plotting of changes in shunt in the critically ill patients was developed. Shunting was determined from simultaneously drawn samples of arterial and mixed venous blood and end-expired air. Cardiac output was determined by the Fick principle and FRC by closed-circuit helium dilution. *Results:* Prior to surgery, the mean total shunt breathing air was 22 per cent and the true shunt while breathing oxygen was 12 per cent. No change in mean total shunt, true shunt, or FRC occurred following surgery. Mean cardiac output for the group, however, was significantly reduced from 6 l/min to 4.8 l/min following surgery and marked individual variation in both cardiac output and $C\bar{v}O_2$–CaO_2 was noted. If these changes had not been taken into account in computing shunt, a significant underestimation of the mean total shunt would have