examined the oxygenation of patients undergoing closed mitral valvulotomy anesthetized with either halothane and oxygen or 50 per cent nitrous oxide and 50 per cent oxygen. The degree of oxygenation was questioned because of inherent lung disease, the lateral position, and thoracotomy. *Method:* Thirteen patients with mitral disease were premedicated with morphine and scopolamine. Control arterial blood samples were taken on room air. The patients were anesthetized with nitrous oxide, halothane and oxygen, intubated and placed in the left chest position. Intermittent hyperinflations were given to minimize atelectasis. At specific times during surgery arterial samples were drawn while the patients were ventilated with 0.5 per cent halothane and 99.5 per cent oxygen. After changing to 50 per cent N_2O, 10 minutes were allowed for equilibration. Then repeat samples were taken. In the recovery room samples were drawn while breathing room air and while breathing 10 liters of oxygen by face mask. The samples were analyzed for P_{O_2}, P_{CO_2} and *p*H using modified Clark, Severinghaus and glass electrodes. *Results:* The degree of ventilation using *p*H and P_{CO_2} as criteria was adequate throughout operation. The mean *p*H under the different circumstances ranged from 7.46–7.50; the mean Pa_{CO_2} from 28 to 35 mm. of mercury. When oxygen and halothane were used the mean Pa_{O_2} was above 300 mm. of mercury. When 50 per cent oxygen and 50 per cent nitrous oxide were given the mean Pa_{O_2} was 195 mm. of mercury with the chest closed, but fell to mean 88 mm. of mercury just before valvulotomy. At this time 9 patients had a Pa_{O_2} below 100 mm. of mercury, 2 were in the 40–50 mm. of mercury range. During closure the mean Pa_{O_2} was 113 mm. of mercury, and 6 patients had a Pa_{O_2} below 100 mm. of mercury. As an index of shunting caused by atelectasis the A-a oxygen tension gradients were calculated using Pa_{O_2}'s when breathing 99.5 per cent oxygen. With the chest closed the mean gradient was 166 mm. of mercury. When the chest was opened the mean gradient rose to 353 mm. of mercury and was 340 mm. of mercury during closure. When oxygen tension was below that necessary to saturate hemoglobin, shunt could not be calculated from A-a tension gradient but was calculated from A-a content gradient. The oxygen contents were calculated from the hemoglobin, P_{O_2} and O_2 saturations utilizing an oxygen dissociation curve in the Handbook of Respiration. On 50 per cent oxygen with the chest open the content gradient was 1.79 volumes per cent as compared to 1.14 volumes per cent on 99.5 per cent oxygen. This difference indicated a significant ($P < 0.02$) increase in shunt caused by uneven ventilation in relation to perfusion. Before operation and in the recovery room the mean arterial P_{O_2} on air was nearly the same, 72 mm. of mercury and 67 mm. of mercury, respectively. Breathing oxygen by mask in the recovery room the mean Pa_{O_2} was 223 mm. of mercury. *Conclusions:* Patients undergoing closed mitral valvulotomy need more than 50 per cent oxygen in the inspired air. In spite of intermittent deep breaths shunting due to atelectasis was considerable and doubled when the chest was opened. When 50 per cent nitrous oxide was used with the chest open there was a significant increase in shunting due to the maldistribution effect. In the recovery room oxygen by mask allowed the full saturation of hemoglobin.

The Central and Peripheral Effects of Halothane Upon Respiration in Man. YONG H. HAN, M.D., HARRY J. LOWE, M.D., JOHN L. EVERS, PH.D., MARTIN I. GOLD, M.D., and MARTIN HELRICH, M.D., *Roswell Park Memorial Institute, Millard Filmore Research Institute, Buffalo, New York, and Department of Anesthesiology, University Hospital, University of Maryland, Baltimore, Md.* The ventilatory response to CO_2 (VR_{CO_2}) in man has been studied extensively under various conditions by numerous investigators employing many methods. The methods employed do not distinguish between central and peripheral effects of drugs, but measure the combined effects. The technique for determining central regulation of respiration during general anesthesia may be modified to differentiate central and peripheral effects. This modification is a comparison of the apneic threshold VR_{CO_2} with spontaneous VR_{CO_2} during periods of: (1) the awake resting control state, and (2) anesthesia. The apneic threshold may be defined as the arterial *p*H and P_{CO_2} at which spontaneous breathing

ceases. This can be attained and maintained by the technique of alternate brief periods of assisted and controlled ventilation. (Elam, J. O., and others: New York J. Med. 59: 4543, 1959; Fink, B. R., and others: ANESTHESIOLOGY 23: 200, 1962). In the present study, the central and peripheral effects of halothane on respiration in man are reported. *Method:* Eleven patients with no evidence of cardiorespiratory abnormality were studied preoperatively. Five patients had no premedication, and anesthesia was induced and maintained with halothane-O_2. The remaining 6 patients were given premedication of morphine and scopolamine. In the latter group of 6 patients, 3 were anesthetized with thiopental and halothane-O_2 and 3 with halothane-O_2. No other drugs were given during the test period. Arterial blood halothane concentrations were measured with a flame ionization detector, and the arterial *p*H and P_{CO_2} were determined by an electrometric method. During stable anesthesia the patients were permitted to rebreathe three or four different concentrations of CO_2 by partially bypassing the CO_2 absorber. Inspired and end-expired alveolar P_{CO_2} were measured continuously by an infrared CO_2 analyzer. Alveolar ventilation was obtained by graphic analysis of the CO_2 and pneumotachographic flow records. A mechanical ventilator was used to assist ventilation during the determination of apneic threshold VR_{CO_2}. *Results:* The spontaneous ventilatory response to CO_2 (VR_{CO_2}) was depressed in 11 patients whose blood levels of halothane ranged from 6.2 to 12.3 mg. /100 ml. The decrease in slope and lateral displacement of the spontaneous VR_{CO_2} were directly related to the blood halothane concentration. The slope of the apneic threshold VR_{CO_2} during the tested concentrations of halothane anesthesia was approximately the same as that of the awake resting control VR_{CO_2}. These data indicate that depressed spontaneous VR_{CO_2} under halothane anesthesia is mainly due to peripheral factors. During the steady state of halothane anesthesia with opiate premedication (with or without thiopental induction) the slope of apneic threshold VR_{CO_2} was less than that of the awake control VR_{CO_2}. This indicates that the decreased spontaneous VR_{CO_2} under these conditions is mainly due to central factors. *Conclusions:* During halothane anesthesia, spontaneous ventilatory response to CO_2 is depressed in direct relation to blood halothane levels. Such depressed respiration is mainly due to peripheral factors. However, when opiate premedication, with or without a thiopental induction is used, depression of respiration is chiefly due to central factors. The evidence suggests that central and peripheral effects of drugs on respiration may be differentiated by this method. (Dr. Y. H. Han is presently at the Department of Anesthesiology, University Hospital, University of Maryland, Baltimore.)

Effect of Anesthetic Drugs on Central Nervous System Toxicity of Hyperoxia. J. R. HARP, M.D., B. B. GUTSCHE, M.D., and C. R. STEPHEN, M.D. Oxygen pressures employed in hyperbaric surgery, 3–4 atmospheres (ATA), rapidly produce acute central nervous system toxicity. Seizures and death overshadow the more gradually appearing pulmonary damage (Stadie, W. C., and Hangaard, N.: Amer. J. Med. Sci. 207: 83, 44). Anesthetic drugs have been shown to delay or prevent the development of seizures in animals exposed to hyperbaric oxygen (Bean, J. W.: Physiol. Rev. 25: 1, 45). Recent observations indicate these same drugs may increase severity of delayed oxygen toxicity of the central nervous system. (van den Brenk, H. A. S., and Jamieson, D.: Biochem. Pharmacol. 13: 165, 64). *Method:* Our initial experiments were designed to parallel potential clinical settings. Mongrel dogs weighing 10–15 kg. were anesthetized with halothane (6 dogs), thiamylal (5 dogs), or paralyzed without anesthesia with succinylcoline (5 dogs). Endotracheal intubation was performed and catheters inserted into femoral artery and jugular vein employing local anesthesia in the succinylcholine group. All animals in this latter group were ventilated with a Harvard pump respirator twenty times per minute with tidal volume of 25 ml./kg. One animal in the halothane series and 2 animals in the thiamylal series had respirations assisted with a Bird Mark 8 mechanical ventilator. In the remaining animals, spontaneous respirations were maintained. EEG, ECG and arterial pressure were continually monitored on an E and M recorder. Arterial and venous