mal Pa_{O_2}; however, because of the tendency towards hypercarbia and acidosis, respiration should be assisted intermittently during anesthesia.

A Radical Approach to Therapy for the Pulmonary Complications of Cystic Fibrosis. PAUL R. HACKETT, M.D., and HERMAN W. REAS, M.D., *Washington University, School of Medicine, St. Louis.* The abnormal mucoprotein produced in cystic fibrosis is highly viscid. Ineffective removal of secretions in the tracheobronchial tree is responsible for the sequence of: obstruction of terminal bronchioles, emphysema, atelectasis, infection and chronic bronchitis, bronchiectasis and pulmonary fibrosis. Pulmonary function changes begin as diminished ventilation due to obstruction. As lung destruction proceeds the alteration of function becomes restrictive and irreversible. Functional residual capacity (FRC) is increased, with a decreased expiratory reserve volume (ERV) and inspiratory capacity (IC). Forced vital capacity (FVC) is reduced. If retained secretions can be removed, the progression of pulmonary disease can be halted. N-actylcysteine is a new, effective mucolytic agent. Its activity depends on the free sulfhydryl group which reduces the disulfide linkages of mucoprotein, decreasing its viscosity. Studies by Reas on mucus from two patients with cystic fibrosis showed a 90 to 95 per cent reduction in viscosity after the inhalation by nebulizer of 20 per cent N-acetylcysteine twice daily. Based on these data, he began treating pulmonary complications of cystic fibrosis by nebulization of N-actylcysteine twice daily followed by postural drainage and clapping. Success was most apparent in children with primarily obstructive disease. If conservative care was not effective, a more radical approach was adopted; tracheobronchial toilet under general anesthesia. *Indications:* The technique is used in progression of lung infiltrates, rapid deterioration of pulmonary function, and cardiac failure. *Rationale:* Direct instillation of N-acteylcysteine and tracheobronchial toilet is possible. Removal of secretions from major bronchi followed by nebulization and controlled hyperventilation will deposit N-acetylcysteine deep in the small bronchi. Atelectatic segments may be inflated after treatment. Improvement in ventilation makes continued conservative care more effective. *Method:* Anesthesia was induced in 35 procedures with methohexital and maintained with equal parts of nitrous oxide and oxygen. Intermittent succinylcholine was used as necessary. The trachea was intubated and 10 ml. of 20 per cent N-acetylcysteine was instilled with the patient in four positions; *i.e.*, supine, steep Fowler's, right and left lateral. Tracheobronchial toilet and positional drainage removed gross secretions. Twenty per cent N-acetylcysteine was then nebulized for an hour utilizing a no. 42 DeVilbiss nebulizer in a modified Ayres T-circuit. Hyperventilation was carried on throughout the procedure. On return to the ward, the child was placed in a mist tent for 12 hours. Meticulous attention to hydration and electrolyte balance during this entire period was important. *Results:* There was a significant improvement in pulmonary function. The FVC PVC ratio (forced vital capacity/predicted vital capacity) increased an average of 19 per cent. The most dramatic improvement was in the expiratory reserve volume (ERV/FVC ratio increased 11 per cent). Atelectatic segments were re-expanded, bronchietatic sacs were emptied and pneumonitis was cleared. Improvement was also seen as a consistent increase in arterial oxygen saturation and a decreased P_{CO_2}. Cyanosis disappeared, food intake improved, growth was resumed and these children subjectively improved as activity increased. *Conclusion:* Our experience with 35 procedures in severely ill patients has encouraged us to approach the problem of retained secretions more aggressively. Certainly, any child with cystic fibrosis who requires anesthesia for surgery should undergo the described procedure to prevent serious postoperative pulmonary complications.

Oxygenation During Closed Mitral Valvulotomy with Halothane and Nitrous Oxide Anesthesia. PHILLIPS HALLOWELL, M.D., JOHN HEDLEY-WHYTE, M.B., W. GERALD AUSTEN, M.D., and MYRON B. LAVER, M.D., *Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, the Department of Surgery, Harvard Medical School, and the General Surgical Services, the Massachusetts General Hospital.* This study

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