ples to monitor the adequacy of ventilation during operation

Cerebral Effects of Induced Electroencephalographic Seizures in Dogs. LESTER C. MARK, M.D., and LEONARD BRAND, M.D., *Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, New York.* Sustained convulsions may result in severe hypoxia from inability of respiratory muscles to function synchronously. Adequate ventilation cannot readily be achieved until convulsions are interrupted with barbiturates or muscle relaxants. Barbiturates suppress both visible motor hyperactivity and electroencephalographic (EEG) activity. With relaxant drugs EEG convulsive discharges continue despite inability of muscles to contract. A useful monitor is thus available for relaxant therapy of status epilepticus: cessation of paroxysmal EEG seizures serves notice that relaxant therapy may safely be withdrawn (James and Whitty: Lancet *2:* 239, 1961). There is evidence that cerebral oxygen tension decreases during seizures even before hypoxemia develops (Clark and others: J. Appl. Physiol. *13:* 85, 1958; Meyer and Gotoh: Physiologist *3:* 113, 1960). This report attempts to establish whether continuing electrical seizure activity in the brain is itself harmful. *Method:* A series of ten paired experiments was performed in eight mongrel dogs weighing 5 to 12.5 kg. Each dog was paralyzed with succinylcholine 2 mg./kg. intravenously and respired mechanically with room air via an endotracheal tube. Procaine 100 mg./kg. was injected intravenously in 15 seconds. The paralyzed dog did not convulse, but within 15 to 30 seconds EEG waves of high amplitude and slow frequency appeared, progressing within two minutes to paroxysmal activity alternating with periods of burst suppression. Gradually EEG paroxysms began to recur less frequently and grew shorter, disappearing in 15 to 45 minutes. Silent periods were replaced by increasing electrical activity until final reversion to control patterns, when dogs were usually active and awake. During return to full activity, appearance times of muscular twitching, adequate spontaneous respiration, righting reflex, and inability to walk were noted. A week or more later, the procedure was repeated with the same dog, except that EEG seizures were suppressed two minutes after onset by thiopental, 100 mg. intravenously. The same recovery end points were noted. In some pairs experimental sequence was reversed, but each dog always acted as his own control. Two dogs were used for two pairs of experiments. In another experiment five dogs received succinylcholine, and one received thiopental, in standard doses; no procaine was administered. Recovery times for each animal were usually significantly shorter than following procaine convulsions. *Results:* Patterns of recovery varied, both in time of first appearance of spontaneous movement and in total time required for the sequence until ability to walk unaided. However, behavior of any individual dog was consistent and reproducible from experiment to experiment, with thiopental or without. In ten paired convulsion experiments, no significant difference appeared in recovery times for each animal whether EEG seizure activity was aborted with thiopental or terminated spontaneously. Between experiments, dogs appeared normal with no evidence of neurological deficit or personality change. *Conclusion:* It is concluded that paroxysmal EEG seizures allowed to disappear spontaneously cause no apparent harm to dogs whose lungs remain well ventilated. Room air seemed adequate. Whether these findings apply to man, where psychological tests are available to detect subtle changes in personality, has not been determined.

Adverse Effects on the Newborn of Severe Maternal Hyperventilation. H. MORISHIMA, M.D., PH.D., F. MOYA, M.D., A. BOSSERS, M.D., and V. THORNDIKE, M.D., *Department of Anesthesiology, College of Physicians and Surgeons, Columbia University and the Presbyterian Hospital, New York, New York.* Recent investigations have shown that the acid-base status of the fetus and newborn tends to reflect changes in maternal P_{CO_2}, *p*H, and bicarbonate. Most previous work has been concerned with the production of metabolic acidosis in the mother through the administration of ammonium chloride. A close direct correlation between maternal and umbilical-vein *p*H values was noted. At the Sloane

Hospital for Women, we have investigated the effects of hyperventilation on the human mother and her infant. It appears that moderate shifts in maternal acid-base balance toward alkalosis are reflected in the infant at birth by an improvement in his acid-base status. However, above a maternal *p*H of 7.55 the infant ceases to follow the mother, and at a *p*H level of about 7.68 actual adverse changes were observed in the biochemical status as well as the clinical condition of three infants. The present study was designed to determine the influence of severe maternal hyperventilation and respiratory alkalosis upon the acid-base status of the newborn animal, and to relate these data to the phenomena observed in the human being. *Method:* Forty-three pregnant guinea pigs near term were divided into two groups: the first group breathed spontaneously, while the second group was hyperventilated by controlled respiration during the study period. Immediately following cesarean section umbilical cords were clamped before the piglets started to breathe. Maternal and newborn *p*H, P_{CO_2}, buffer base, and hematocrit value were determined in simultaneous samples taken from the maternal carotid artery and the placental side of the clamped umbilical vein. *Results:* The mothers in the control group had a mean arterial *p*H value of 7.43 and a mean P_{CO_2} of 34.8 mm. of mercury. In the hyperventilated group the mean values were 7.75 and 14.6 mm. of mercury, respectively. The respiratory origin of the alkalosis was confirmed by the linear relationship of the P_{CO_2} values to blood *p*H. The umbilical vein blood in the hyperventilated group had a mean *p*H of 7.05, which was clearly lower than the control group. The *p*H gradient between maternal and cord blood was also higher in the hyperventilated group. Furthermore, statistically-significant elevation of P_{CO_2} and depresison of buffer base were found in the umbilical vein samples of the hyperventilated group. The clinical status of the newborn animals was assessed by a scoring system similar to the Apgar score used in human infants. The piglets of the hyperventilated group had low scores, which appeared to be related to the increased *p*H gradients between maternal and cord blood. *Conclusion:* It was concluded from these observations that placental perfusion diminished with hyperventilation, perhaps as a result of vasoconstriction associated with severe alkalosis in the mother. This is indicated by the findings of low *p*H, high P_{CO_2} and lowered buffer base in umbilical vein blood of the hyperventilated group. [This work was supported in part by research grants from the National Institutes of Health, the Public Health Service (RG-9069, formerly H-2410 and H-5877 (R1).]

Effect of Trichlorethylene and Methoxyflurane on Central Respiratory Mechanisms. S. H. Ngai, M.D., R. L. Katz, M.D., and D. C. Brody, M.D., *Departments of Anesthesiology and Pharmacology, College of Physicians and Surgeons, Columbia University, New York, New York.* Recent studies in our laboratory (Fed. Proc. *21:* 328, 1962) indicated that diethyl ether is primarily a respiratory depressant. In decerebrate cats diethyl ether caused a transient tachypnea which was abolished by vagotomy. Continued inhalation of this agent progressively decreased the respiratory amplitude and minute volume. Ventilatory response to CO_2 inhalation decreased. The medullary inspiratory center became less responsive to electrical stimulation. Prolonged inhalation of diethyl ether led to a secondary tachypnea which was related to the development of acidosis. The present report deals with parallel studies with trichlorethylene and methoxyflurane. *Method:* In cats 60 to 90 minutes after decerebration, oxygen or anesthetic mixture was inhaled through a non-rebreathing system. Ventilation was measured with a Servo-spirometer. Respiratory movements were registered with a thoracic pneumograph. Arterial pressure was measured from the femoral artery with a Statham transducer. Recordings were made on a Grass polygraph. Arterial blood samples were obtained for analysis of *p*H and P_{CO_2} (Astrup). In some experiments the medullary inspiratory center was electrically stimulated before and during anesthesia to determine the stimulus threshold and maximal response. *Results:* One per cent trichlorethylene progressively increased respiratory rate and decreased respiratory amplitude. The minute volume generally increased, but this change was not consistently observed. There was either no change or a