The Effects of Anesthetics on the Release of Norepinephrine from Sympathetic Nerves. S. H. NGAI, M.D., SIDNEY OZERNITSKY, M.D., and P. M. DIAZ, M.D., *Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, N. Y.* Biosynthesis, uptake and release of norepinephrine in the peripheral sympathetic nervous tissue play important roles in circulatory homeostasis. Differences among anesthetics in their action on these mechansims could well explain their varied effects on the circulation. The present study deals with the release of norepinephrine as affected by anesthetics, particularly cyclopropane. *Method:* One series of experiments was carried out in dogs anesthetized with chloralose (100 mg./kg., intravenously). The chest was opened through a midline sternotomy. The coronary sinus outflow was diverted with a modified Morawitz cannula, measured with an electromagnetic flowmeter and returned to the right atrium. The arterial pressure was measured with a Statham transducer. A small catheter (PE 50) was inserted retrograde through a branch of the anterior descending coronary artery with its tip placed near the left main coronary artery. The myocardial norepinephrine store was labelled by intraarterial infusion of *dl*-H^3-norepinephrine (100 μC.). Arterial and coronary sinus blood samples were obtained at intervals. After appropriate treatment radioactivity in the plasma water was measured with a liquid scintillating counter. The body temperature was maintained at 38–39° C. with heating blankets. A Frumin-Lee respirator provided constant-volume ventilation. Cyclopropane (15 per cent) or halothane (1 per cent) was administered with a non-rebreathing system after a period of control observation. *Results:* With cyclopropane the pattern of norepinephrine release was not altered in seven of ten animals. In the remaining three radioactivity in the coronary sinus blood increased during inhalation of cyclopropane. Electrical stimulation of the left stellate ganglion raised the arterial pressure and the coronary sinus outflow with a concomitant increase in norepinephrine release. Cyclopropane did not appear to influence these effects of stimulation either. In four animals no change in release of norepinephrine was observed during inhalation of halothane. In another series of experiments using decerebrate cats, the norephinephrine store in the iris was labelled by intracarotid infusion of *dl*-H^3-norepinephrine. The anterior chamber was perfused with Ringer's solution and the radioactivity of effluent perfusate measured. Electrical stimulation of the cervical sympathetic trunk caused a papillary dilation and a release of norepinephrine into the anterior chamber. The magnitude of release became constant after five to seven bouts of stimulation. Cyclopropane caused no change in the response in five of eight animals, a decrease in release in two and an increase in one. *Conclusions:* It may be concluded that under these experimental conditions cyclopropane anesthesia did not increase the release of norepinephrine from the peripheral sympathetic nerves. Studies are being carried out to elucidate further the adrenergic transmitter mechanisms in the periphery. (Supported by USPHS Grants 5T1-GM-00056 and GM-09069.)

A Possible Ventilatory Effect of Carbonic Anhydrase Inhibition Following Topical Sulfamylon in Burned Patients. PAUL J. SCHANER, CAPT., MC; JERRY M. SHUCK, CAPT., MC; CHARLES R. RITCHEY, MAJ., MSC, *US Army Surgical Research Unit, Brooke Army Medical Center, Fort Sam Houston, Texas.* Hyperpnea has been noted frequently in patients with 30 per cent or greater total body burns who are treated with Sulfamylon®. Arterial blood gas studies in these patients disclosed normal to subnormal P_{O_2}, hypocapnia, some degree of base deficit, and normal to alkaline *p*H. Sulfamylon therapy causes carbonic anhydrase inhibition (CAI). The study was undertaken to determine the possible ventilatory effect of prolonged inhibition of carbonic anhydrase (CA) in the burned patient. *Methods:* Patients sustaining a 30 per cent or greater total body burn were studied for as long as 60 hours after the initial application of Sulfamylon. Parameters studied included: inhibition of renal CA as judged by urinary titratable acidity, bicarbonate and ammonium excretion, degree of red blood cell CAI, blood levels of Sulfamylon, arterial *p*H and blood gases, respiratory minute volume, with end-tidal P_{CO_2}. *Results:* Renal CAI

occurred within 45 minutes after application of Sulfamylon. The inhibition resulted in incomplete reabsorption of bicarbonate while ammonium, along with titratable acidity, disappeared from the urine. An alkaline diuresis ensued. In Sulfamylon-treated patients, red blood cell CAI occurred between 12 and 24 hours after renal CAI. A group of controls, fully-recovered burned patients, were given 7.5 mg./kg. body weight of acetazolamide intravenously. They had renal CAI and near 50 per cent red blood cell CAI within an hour. The fully-recovered patients did not have significant alterations of baseline determinations. The 11 Sulfamylon-treated burn patients were followed up for a 24-hour period. Mean admission values included: arterial *p*H 7.45, P_{CO_2} 29.6 mm. Hg, P_{O_2} 76.5 mm. Hg, bicarbonate 20 mEq./l. After 24 hours of Sulfamylon therapy, mean values included *p*H 7.40, P_{CO_2} 26.6 mm. Hg, P_{O_2}: 87.9 mm. Hg, and bicarbonate 17.6 mEq./l. An alkaline shift of arterial *p*H frequently occurred after the first 24 hours of Sulfamylon therapy. Respiratory minute volume increased to a peak within three hours of the start of therapy. Later, a gradual decline in minute volume occurred, but it did not return to baseline. Continued therapy resulted in a maintained elevated minute volume. During the initial 12-hour period, renal CAI was evident while red blood cell CAI was minimal. Red blood cell CA is known to be resistant to inhibition, probably because of the high concentration of the enzyme in the red blood cell (Maren, T. H., *et. al.*: Bull. Johns Hopkins Hosp. *95:* 199, 1954). An impaired CO_2 output from the lung has been shown to occur in man following inhibition of carbonic anhydrase with no change in oxygen uptake (Stromme, J. H., and Fog, J.: J. Appl. Physiol. *19:* 6, 1962). In dogs, intravenous administration of a Sulfamylon compound, at a dose which duplicated patient blood levels during treatment, permitted recovery of this inhibitor of CA in the cerebrospinal fluid. *Conclusions:* Inhibition of central nervous system carbonic anhydrase (CAI) can occur from the effects of sulfamylon. Much evidence supports the contention that intracellular CO_2 build-up mediates the neurophysiologic and neurochemical effects of CAI (Woodbury, D. M., and Korter, R.: ANESTHESIOLOGY *21:* 686, 1960; Gotoh, F., *et al.*: Arch. Intern. Med. *117:* 39, 1966). A rise of tissue P_{CO_2} in the central nervous system plus the inherent metabolic acidosis of renal CAI and/or any impairment of respiratory CO_2 elimination may explain the ventilatory effect of Sulfamylon. Sulfamylon has significantly reduced the mortality of burns covering as much as 60 per cent of total body surface. Before Sulfamylon, burn wound sepsis was the chief cause of mortality in burns; pneumonia has replaced sepsis as the chief cause of mortality. Pneumonia, in the presence of CAI, can result in a rapid demise related to acidosis.

Effect of Thiopental Nitrous Oxide-oxygen Anesthesia on Blood Levels of Glucose, Pyruvate, Lactate and Metabolites of the Tricarboxylic Acid Cycle during Operation. OLGA SCHWEIZER, M.D., WILLIAM S. HOWLAND, M.D. and COLLEEN A. SULLIVAN, M.D., *Memorial Sloan-Kettering Cancer Center, New York, N. Y.* This study continues our investigations of the effects of anesthetic agents on blood levels of glucose, lactate, pyruvate and metabolites of the Kreb's cycle. *Method:* Twenty-five patients were maintained in a light plane of anesthesia with 2.5 per cent thiopental, 50–50 nitrous-oxide-oxygen. No variations from standard anesthetic and fluid replacement methods were employed except for the substitution of saline for glucose solutions. The blood was warmed after three units and 44.6 mEq. of sodium bicarbonate was administered intravenously after every fifth unit. Arterial blood samples, obtained preoperatively, at two-hour intervals, and at the end of operation, were analyzed for hematocrit, oxygen saturation, Pa_{O_2}, *p*H, Pa_{CO_2}, base excess, standard bicarbonate, total carbon dioxide, glucose, pyruvate, lactate, excess lactate, citrate, α-ketoglutarate, malate, acetyl CoA and adenosine triphosphate (ATP). Excess lactate was determined by Huckabee's formula and acid-base values by the Astrup technic. Enzymatic methods were employed for pyruvate, lactate, ATP and components of the Kreb's cycle. *Results:* For analytical purposes the group was subdivided into patients without (11) and those with (14) excess lactate. Age, sex, type and duration of operation,