14 Faulconer, A. J.: Correlation of Concentration of Ether in Arterial Blood With Electroencephalographic Patterns Occurring During Ether-Oxygen and During Nitrous Oxide Oxygen and Ether Anesthesia of Human Surgical Patients. Anesthesiology, 13: 361, 1952.

15 Gellhorn, E.: Circulatory Studies on Anoxemia in Man With Respect to Posture and Carbon Dioxide. Ann. Int. Med., 10: 1267, 1939.

16 Gibbs, F. A., D. A. Williams and E. L. Gibbs: Modifications of the Cortical Frequency Spectrum by Changes in CO_2, Blood Sugar, and O_2, J. Neurophysiol., 3: 49, 1940.

17 Gorlin, R., and B. M. Lewis: Circulatory Adjustments to Hypoxia in Dogs. J. App. Physiology, 1: 180, 1954.

18 Gremels, G., and E. H. Starling: On the Influence of Hydrogen Ion Concentration and of Anoxemia Upon the Heart Volume. J. Physiol., 61: 297, 1926.

19 Harris, A. S.: Terminal Electrocardiographic Patterns in Experimental Anoxia, Coronary Occlusion, and Hemorrhagic Shock. Am. Heart J., 35: 895, 1948.

20 Harrison, T. R., A. Blalock, C. Pilcher, and C. P. Wilson: The Regulation of Circulation, VIII. The Relative Importance of Nervous, Endocrine, and Vascular Regulation in the Response of the Cardiac Output to Anoxemia. Am. J. Physiol., 83: 284, 1927.

21 Heymans, C.: Introduction to the Regulation of Blood Pressure and Heart Rate. American Lecture Series, Monograph in American Lectures in Physiology, Springfield, Illinois, Charles C. Thomas, 1950.

22 Hopkins, A. L., J. Anzola and G. H. A. Clowes, Jr.: A Quantitative Experimental Comparison of the Effects of Severe Hypercapnia on the Brain and Heart, In press: Surgical Forum, Clin. Congress, Am. Coll. Surgeons, Atlantic City, Nov. 1954, W. B. Saunders, Philadelphia.

23 Lennox, W. G., and E. L. Gibbs: Blood Flow in Brain and Leg of Man and Changes Induced by Alteration of Blood Gases. J. Clin. Investigation, 11: 1155, 1952.

24 Maier, H. C., G. W. Rich, and S. Eicher: Clinical Significance of Respiratory Acidosis During Operations. Ann. Surg., 134: 653, 1951.

25 Mathison, G. C.: The Cause of Heart Block Occurring During Anoxia. Heart, 2: 54, 1910.

26 Miller, F. A., E. B. Brown, J. J. Buckley, F. H. Van Berger and R. L. Varco:Respiratory Acidosis: Its Relationship to Cardiac Failure and Other Physiologic Mechanisms. Surgery, 32: 171, 1952.

27 Nahas, G. G., G. W. Mather, J. D. Wargo and W. L. Adams: Influence of Acute Hypoxia on Sympathectomized and Adrenalectomized Dogs. J. Physiol., 177: 13, 1954.

28 Pollock, G. H.: Central Inhibitory Effects of Carbon Dioxide. J. Neurophysiol., 12: 315, 1949.

29 Reid, L. C., H. E. Stephenson, Jr., and J. W. Hinton: Cardiac Arrest. Arch. Surg., 64: 409, 1952.

30 Sealy, W. C., W. C. Young, and J. S. Harris: Studies on Cardiac Arrest. The Relationship of Hypercapnia to Ventricular Fibrillation, J. Thoracic Surg., 28: 447, 1954.

31 Stephenson, H. E., Jr., L. C. Reid and J. W. Hinton: Some Common Denominators in 1200 Cases of Cardiac Arrest. Ann. Surg., 137: 731, 1953.

32 Van Slyke, D. D., and J. M. Neill: The Determination of Gases and Other Solutions by Vacuum Extraction and Manometric Measurement. J. Biol. Chem., 61: 523, 1942.

33 Zeigler, R. F.: Cardiac Mechanisms During Anesthesia and Operation in Patients With Congenital Heart Disease and Cyanosis. Bull. Johns Hopkins Hosp., 83: 237, 1948.

DISCUSSION.—DR. WALTER J. BURDETTE, New Orleans, Louisiana: Drs. Clowes, Hopkins and Glover are to be congratulated on these excellent studies concerning the mechanism of cardiac arrest. We have also been interested in changes in cardiac muscle after arrest due to hypoxia, and have studied particularly the amounts of adenosine nucleotides in the muscle under these circumstances, since the contraction mechanism is initiated by one of them (ATP) and transfer of energy in muscle is accomplished through phosphate bond interrelationships.

Cardiac arrest was produced by steadily increasing hypoxia during a period of one hour. Homogenates of the muscle were made immediately, and nucleotides separated by means of formate, ion-exchange columns. In a series of 15 dogs adenosine triphosphate (ATP) was reduced from 18.1 ± 1.50 to 7.1 ± 1.18 M × 10^{-4}/g.; adenosine diphosphate (ADP) from 10.8 ± 1.2 to 6.1 ± 0.54 M × 10^{-4}/g.; and adenosine monophosphate from 7.1 ± 0.58 to

4.6 ± 0.50 M $\times 10^{-4}$/g. when the content of normal ventricular muscle was compared to that of muscle in arrest.

Normal cardiac rhythm was resumed in one of three patients with cardiac arrest who were treated by injecting ATP and ADP into the left ventricle with the aorta clamped temporarily, in conjunction with massage. Unfortunately death occurred some hours later from cerebral anoxia. This method of resuscitation is therefore not offered as a panacea, but we do believe that this general method of approach should lead to success in correcting deficiencies, as well as in preventing arrest, although the derangement leading to arrest may be very complex.

In closing, appreciation is expressed to Dr. Rives and members of the Association for the privilege of speaking.

DR. GEORGE H. A. CLOWES, JR., Cleveland, Ohio: I was very much interested in Dr. Burdette's remarks. A great deal of work has been done on the biochemical changes that take place in tissues in states of asphyxia, and in states of pure hypercapnea or pure hypoxia. It is very important to differentiate them, because, as Dr. Dripps and others have pointed out, CO_2 is essentially a narcotizing agent, whereas oxygen lag actually works by depriving the organism of the essential mechanism of energy production.

I take it that Dr. Burdette's observations were made on a state of asphyxia, that is, a combination of both oxygen lack and CO_2 excess, but presumably the effects that he reports are largely those of hypoxia. This and many other chemical effects have been demonstrated to occur below a critical level. Dr. Baird Hastings and his group in Boston, for example, have shown that potassium transfer takes place from cells, made hypoxic, only when the oxygen concentration falls below 20 per cent of normal.