ANGIOTENSIN Angiotensin II, given intravenously in doses of 40–50 μg./100 Gm. body weight, produces an increase in the capacity of the adrenal to synthesize aldosterone, but increase in the production of corticosterone is not significant. Such changes occur about 24 hours after the last injection of angiotensin II and after the circulatory effect of the drug has ceased. (*Glaz, E., and Sugar, K.: The Effect of Synthetic Angiotensin II on Synthesis of Aldosterone by the Adrenals, J. Endocr. 24: 299 (July) 1962.*)

VASOPRESSIN Under physiologic conditions of stress, there is normally an outpouring of antidiuretic substance. In these circumstances, its coronary constricting action is over-ridden by a predominantly sympathomimetic autonomic activity; however, if conditions lead to excessive parasympathomimetic tone, the effects of vasopressin on cardiac function may be deleterious. (*Kramer, J., and others: Role of Vasopressin in Cardiac Arrests, Amer. J. Surg. 104: 664 (June) 1962.*)

CATECHOL AMINES During air breathing the levels of circulating norepinephrine had to be increased at least 13 times above control level to duplicate the pulmonary arterial pressor response to acute hypoxia. In intact man the infusion of norepinephrine elicited pulmonary arterial hypertension by a mechanism different from that of acute hypoxia. The pressor response to acute hypoxia arose from an increased pulmonary vascular resistance. The pressor response to norepinephrine originated primarily in back pressure from the left heart without an increase in pulmonary vascular resistance. Levels of circulating norepinephrine that were insufficient to increase the pulmonary wedge pressure did not exaggerate the pulmonary arterial pressor response to acute hypoxia. Depletion of the pulmonary vascular nerve endings of norepinephrine by reserpine in dogs did not prevent the usual pulmonary arterial pressor response to acute hypoxia. No evidence was found for a role of either epinephrine or norepinephrine in the pulmonary arterial response to acute hypoxia of moderate degree. (*Goldring, R. A., and others: Catecholamines in the Pulmonary Arterial Pressor Response to Acute Hypoxia, J. Clin. Invest. 41: 1211 (June) 1962.*)

CATECHOL AMINES In the dog chlorpromazine and reserpine act differently, both as to site and mechanism. Using quick freeze techniques, the noradrenalin and adrenalin contents of frontal cortex, hypothalamus, hippocampus and the ascending reticular formation of the midbrain were studied. Small doses of chlorpromazine (less than 5 mg./kg.) raised catechol-amine concentrations in all areas, while larger doses reversed this effect with 25 mg./kg., reducing noradrenalin in all areas except the hypothalamus. The rise in adrenalin was greater than noradrenalin and was particularly high in midbrain and hippocampus. Reserpine, 2 mg./kg., depleted catechol amines in all areas, being greatest for noradrenalin, particularly in the midbrain and frontal cortex. (*Malhotra, C. L., and Prasad, K.: Effect of Chlorpromazine and Reserpine on the Catechol Amine Content of Different Areas of the Central Nervous System of the Dog, Brit. J. Pharmacol. 18: 593 (June) 1962.*)

RESERPINE Heart papillary muscle from cats pretreated with 10 mg./kg. body weight of reserpine was studied *in vitro* for the response to subsequently-given ephedrine. The outstanding effect was the inability of the post-reserpine preparation to exhibit the usual spontaneous beat following ephedrine and a diminished positive inotropic action. The peak contraction height and the rate of muscle failure was uninfluenced by reserpine, as was the contractile response to 0.1 μg./ml. of adrenalin. Since reserpine depletes cat heart catechol amines, it is reasoned that the inability of ephedrine to initiate spontaneous beating under these circumstances is due to its action through release of these amines. Because adrenalin causes spontaneous beating in papillary muscles not responsive to ephedrine, blockade of cardiac adrenergic receptors by reserpine was not contributory. (*Cariroli, V. J., Riley, J. F., and Robert, J.: Effect of Reserpine Pre-treatment on the Response of Isolated Papillary Muscle to Ephedrine, Brit. J. Pharmacol. 18: 588 (June) 1962.*)

NEOSTIGMINE EXCRETION A method was described for the quantitative estimation of neostigmine and pyridostigmine in urine by colorimetric determination of the respective

bromophenol-blue complexes. In six myasthenic patients given neostigmine by mouth, less than 5 per cent of the drug was excreted in the urine unchanged, while six similar patients given pyridostigmine by mouth excreted 2 to 16 per cent of this drug. On the other hand, two myasthenic patients given neostigmine intramuscularly excreted up to 67 per cent of the drug in the urine. It would appear neostigmine is partially metabolized in the alimentary tract and that it is less readily absorbed than pyridostigmine. (*Nowell, P. T., Scott, C. A., and Wilson, A.: Determination of Neostigmine and Pyridostigmine in the Urine of Patients with Myasthenia Gravis, Brit. J. Pharmacol. 18: 617 (June) 1962.*)

POTASSIUM DEPLETION The weight of available clinical and experimental evidence does not support the thesis that prolonged administration of benzothiadiazine drugs produces a significant depletion of body potassium, other than an initial transient phase. Renal compensatory mechanisms subsequently lead to readjustments, so that the chronic hypokalemia which may be present represents a deviation from the normal intracellular-extracellular potassium concentration gradient and not a total depletion. It is a relatively benign state, except for its possible potentiation of digitalis toxicity. Deliberate routine supplementation of potassium intake over long periods of therapy with benzothiadizine drugs is unjustified. (*Weller, J. M.: Potassium Depletion and Benzothiadiazine Drugs—A Source of Over-Concern?, Amer. Heart J. 63: 842 (June) 1962.*)

INTRAMUSCULAR SUCCINYLCHOLINE The intramuscular injection of 0.75 mg./kg. succinylcholine chloride, dissolved in water, to ten conscious human subjects caused, within five minutes, an average 70 per cent decrease in grip strength and a 40 per cent decrease in vital capacity. Both parameters returned to control values within 15 minutes. The intramuscular injection of 4 mg./kg. succinylcholine, dissolved in water, to ten lightly anesthetized subjects caused apnea in nine within an average time of two minutes and 35 seconds. The average duration of apnea was 14 minutes and 41 seconds, and respiratory tidal volume returned to control values within an average time of 30 minutes and 19 seconds. The same dose of succinycholine, dissolved in saline, caused apnea in only three of ten anesthetized subjects in four minutes and 13 seconds. The development of the maximum decrease of respiratory tidal volume in the remaining seven subjects was delayed beyond ten minutes and averaged 60 per cent of control. The average duration of the respiratory depression was 33 minutes and 33 seconds. The differences between succinylcholine dissolved in water and dissolved in saline are probably due to different speed of absorption. The intramuscular administration of a 4 mg./kg. succinylcholine dissolved in water to a cirrhotic patient with low plasmacholinesterase activity caused apnea of 51 minutes and respiratory depression of 80 minutes duration. (*Foldes, F. F., and others: Experimental Studies with Intramuscular Succinylcholine in Conscious and Anesthetized Subjects, Der Anaesthesist, 11: 144 (May) 1962.*)

BARBITURATE METABOLISM Paper chromatographic studies of urine and plasma in 18 dogs showed different metabolic pathways for n-methyl-butabarbital and n-methyl-thio-butabarbital. While N-methyl-butabarbital is detoxified by side chain oxidation and demethylation, the N-methylated thiocompound is metabolized by destruction of the barbituric acid ring. The faster recovery after N-methylated thiobutabarbital, in contrast to thiobutabarbital is explained on this particular pathway of detoxification, rather than redistribution factors. (*Frey, H. H.: Untersuchungen über das Schicksal eines N-methyl-thiobarbiturates im Organismus, Arch. Int. Pharmacodyn. 134: 175 (Nov.) 1961.*)

NEUROMUSCULAR BLOCKADE AND EEG Sleep may be the result of deafferentation of the cortex, with resulting electrocortical synchronization. Desynchronization is characteristic of the awake state. The administration of neuromuscular blocking agents should reduce afferent impulses from muscles, tendons, and joints, and should predispose to somnolence. Somnolence and electrocortical synchronization were produced by the intravenous administration of Flaxedil, or Flaxedil plus barbiturate. Intracarotid injection did not have the same effect, showing that this