TOXICITY The influence of hydergine, chlorpromazine, promethazine and meperidine on the toxicity of procaine, procaine amide and tetracaine was studied in 860 mice. Different combinations of chlorpromazine, meperidine and promethazine increase the toxicity of procaine. Addition of hydergine causes a lesser increase of toxicity. The classical cocktail also increases the toxicity of tetracaine. (*Wellhöner, H. H., and others: Change of Toxicity of Procaine Amide and Tetracaine by Components of Lytic Mixtures. Der Anaesthesist 8: 235 (Aug.) 1959.*)

VAGAL INHIBITION The action of morphine (0.1 to 100 mg./kg.) on the cardiac slowing produced by stimulation of the right vagus nerve varied in the four species studied. In the guinea pig, morphine had no inhibitory effect and in the cat the effect was small, but in the rat and the rabbit stimulation of the vagus slowed the heart much less after administration of morphine than before. In the last two species morphine delayed the onset of cardiac slowing. Nalorphine, which, given alone had a slight morphine-like action, partly reversed the effect of morphine. (*Kosterlitz, H. W., and Taylor, D. W.: Effect of Morphine on Vagal Inhibition of Heart, Brit. J. Pharmacol. 14: 209 (June) 1959.*)

PRESSOR AMINES Methylphenidate, a central nervous system stimulant, can alter the pressor responses in the dog to a series of phenylalkylamines. The amines are affected in three different ways. They may be (1) potentiated or not altered, (2) reversibly blocked, or (3) irreversibly blocked. Differences in structure of the phenylalkylamines may be some of the factors involved. (*Povalski, H. J. and Goldsmith, E. D.: Effect of Methylphenidate on the Cardiovascular Actions of Pressor Amines, Proc. Soc. Exp. Biol. & Med. 101: 717 (Aug.–Sept.) 1959.*)

ISOPROTERENOL Six patients with complete heart block and one with a 2:1 block were given graded doses of isoproterenol and data collected with dynamic recording systems to evaluate the hemodynamic effects of the drug, in contrast to the already known effects on the cardiac conduction system. After isoproterenol average cardiac index increased from 2.45 liters to 3.58 liters. Average resting ventricular rate increased from 40.7 to 45.8 beats per minute. Stroke volume increased on an average of 32.2 per cent. Average left ventricular work rose from 4.52 to 7.19 kg.-meters/minute. Left ventricular stroke work was also increased. The data would indicate that sublingual isoproterenol has both a chronotropic and inotropic effect on both heart block and normal hearts. (*McGaff, C. J., Cohen, H. K., and Leight, L.: Hemodynamic Effects of Isoproterenol in Complete Heart Block, Arch. Int. Med., 104: 242 (August) 1959.*)

CATECHOL AMINES Both local and systemic lesions can be produced by the administration of epinephrine and norepinephrine. Two different mechanisms are responsible for pathologic changes. One is mechanical, due to hemodynamic factors; the other is chemical, producing derangement in cellular oxidation by uncoupling oxidation phosphorylation. Best examples of the first mechanism are the massive cerebral hemorrhage and hemorrhage into the mitral valve. These lesions depend more on the rapidity of infusion than on total dose. The second mechanism is best illustrated by the myocardial necrosis following prolonged dosages of norepinephrine, not associated with marked changes in blood pressure. Hemodynamic changes combine with the hypoxiating effects of norepinephrine in the production of lesions of the liver, kidneys, and large vessels. In the production of skin necrosis, the additional factors of hydrostatic pressure of the infiltrating fluid and local anatomic peculiarities are important. (*Szakacs, J. E., and others: Pathologic Implication of Catechol Amines, Epinephrine and Norepinephrine, U. S. Armed Forces Med. J. 10: 908 (Aug.) 1959.*)

PREMEDICATION The administration of morphine 10 mg. and scopolomine 0.4 mg., one and a half hours prior to anesthesia, produces an air of indifference with amnesia without circulatory and respiratory depression. This is superior to preanesthesia sedation from barbiturates. Because of its hypotensive action, the authors are reluctant to anesthetize anyone who has received chlorpromazine or any of its allies of similar potency within 48

hours of operation. Since so little advantage is accrued from the use of tranquilizers in addition to the narcotics, the addition of a third drug is not recommended. Levohyoscyamine is more effective than scopolomine or atropine for suppressing vagal activity. (*Adriani, J., Webb, C., and Steiner, L.: Pre-Anesthetic Medication: 1958 Concepts, South. M. J. 52: 1137 (Sept.) 1959.*)

HYALINE MEMBRANE Contamination of the amniotic fluid with blood at time of incision of the uterus stands out as the chief factor in the formation of hyaline membranes in the air passages of the newborn. In a series of 56 infants delivered by cesarean section at term, microscopic examination of the lungs showed contamination of bronchioles and alveoli with blood in more than 90 per cent. Fetal breathing before incision of the uterus was evidenced by contamination of the air passages by foreign matter in those stillborn infants who had died during labor with ruptured membranes. The highest incidence of hyaline membrane formation was in those infants delivered before labor, rather than in those delivered during labor. (*Snyder, F. F.: Pulmonary Hyaline Membrane, Obst. & Gynec. 14: 267 (Sept.) 1959.*)

PAIN In a series of experiments on frogs and human volunteers it was found that pain producing stimuli caused the release of intracellular potassium which is a pain-producing stimulus. If the potassium releasing process was inhibited or neutralized by calcium or reversed by increasing cellular uptake of potassium by means of a glucose-insulin combination, the response to painful stimuli was decreased. The major effect of a noxious stimulus is not the direct effect on the pain receptor but is indirect due to tissue reaction. (*Benjamin, F. B.: Release of Intracellular Potassium as Physiological Stimulus for Pain, J. Appl. Physiol. 14: 643 (July) 1959.*)

METARAMINOL SLOUGH Tissue necrosis and slough occurred in the leg of a patient with severe atherosclerosis who was subjected to a slow intravenous infusion of metaraminol (Aramine). Concentrations of the agent were not excessive (75 mg. of metaraminol in 2,600 cc. of isotonic dextrose), but subcutaneous extravasation occurred along the course of the vein. Multiple intramuscular injections in the adequately vascularized upper arms and shoulders had been well tolerated, as had been the case with intravenous infusions and one episode of subcutaneous infiltration. However, any potent vasoconstrictor drug, when used in the presence of arterial insufficiency, is a potential cause of tissue necrosis. When metaraminol is used, all precautions against tissue damage, such as polyethylene catheters and phentolamine (Regitine) in the local area after extravasation, should be utilized, particularly in the presence of vascular insufficiency. (*Dippy, W. E., and Dorney, E. R.: Tissue Necrosis and Slough Produced by Metaraminol Bitartrate, J. A. M. A. 170: 1647 (Aug. 1) 1959.*)

SHOCK A very significant elevation in plasma lactic dehydrogenase (LDH) activity occurs in experimental hemorrhagic shock in dogs. An initial lag period is followed by a sharp rise, 15–50 times the original value. Such a rise bears a consistent relationship to rate of spontaneous return of blood from the reservoir to the animal ("taking up") and reversibility to replacement transfusion. Studies suggest that serial plasma LDH determinations may prove to be helpful indicators of the extent of biological deterioration in hemorrhagic shock. (*Vessell, E. S., and others: Plasma Lactic Dehydrogenase Activity in Experimental Hemorrhagic Shock, Proc. Soc. Exp. Biol. & Med. 101: 644 (Aug.–Sept.) 1959.*)

SHOCK Reversible and irreversible shock can be caused by intravascular thrombi in the following manner: (a) reversible shock may be due to a decreased cardiac output secondary to an acute cor pulmonale resulting from blockage of pulmonary capillaries with thrombi and associated serotonin-produced vascular spasm or to a damming of blood in the portal system due to thrombi in the liver and associated vascular spasm. (b) Irreversible shock may be due to a loss of blood and serum into the gastrointestinal tract secondary to hemorrhagic necrosis of the bowel mucosa caused by an episode of intravascular clotting in the bowel mucosa and submucosa. (*Hardaway, R. M.,*