the untoward side effects of the latter. (*Chilton, N. W., Lewandowski, A., and Cameron, J. R.: Double-Blind Evaluation of New Analgesic Agent in Post-Extraction Pain, Amer. J. Med. Sci. 242: 702 (Dec.) 1961.*)

PRESSOR AMINES A new technique for simultaneously measuring total myocardial blood flow and cardiac output with the (dog) heart intact and functioning in a physiological manner has been developed using radioiodinated (I^{131}) human serum albumin. When given to hypovolemic dogs, norepinephrine caused a substantially greater blood flow through the myocardium than did any other amine tested. This ability of norepinephrine to increase myocardial flow was followed in order of decreasing effectiveness by metaraminol, epinephrine, and phenylephrine. Since there was little or no change in myocardial blood flow when phenylephrine was used to raise blood pressure, it can be assumed that this drug causes about the same degree of vasoconstriction in the coronary arteries as it does in the systemic vessels. In contrast, the effects of norepinephrine, metaraminol, and epinephrine on myocardial blood flow are due to coronary vasodilation as well as to systemic vasconstriction. (*Dunn, H. K., and others: Effect of Pressor Amines on Myocardial Blood Flow in Dog, J. A. M. A. 178: 1090 (Dec. 16) 1961.*)

NOREPINEPHRINE After the intravenous administration of H^3-norepinephrine, it was taken up by the heart and slowly released over a period of days. Long-acting monoamine oxidase inhibitors blocked the slow release of H^3-norepinephrine. Long-acting and short-acting monoamine oxidase inhibitors blocked the releasing action of reserpine on H^3-norepinephrine in the heart. On the basis of these observations it is proposed that monoamine oxidase inhibitors elevated the catechol-amine concentration in certain tissues by blocking the release of the hormone from its binding site. (*Axelrod, J., Hertting, G., and Patrick, R. W.: Inhibition of H^3-Norepinephrine Release by Monoamine Oxidase Inhibitors, J. Pharmacol. Exp. Ther. 134: 325 (Dec.) 1961.*)

NOREPINEPHRINE UPTAKE Tyramine, amphetamine, cocaine, chlorpromazine, imipramine, reserpine, guanethidine and dibenzyline (phenoxybenzamine) markedly reduced the concentration of administered H^3-norepinephrine in the heart, spleen and (except for guanethidine) adrenal gland. These drugs lowered the H^3-catechol-amine concentration to a moderate degree in the liver. Imipramine was the only drug that lowered the H^3-catechol-amine in skeletal muscle. The level of H^3-normetanephrine was decreased by all these drugs in heart and spleen and in some cases in the adrenal gland and liver. Tyramine, amphetamine, cocaine, chlorpromazine, imipramine, reserpine, guanethidine and dibenzyline also elevated the plasma levels of administered H^3-norepinephrine for the first 5 minutes. The plasma levels of H^3-normetanephrine were also raised to varying degrees. These drugs appear to be acting by preventing the entry and/or the binding of H^3-norepinephrine. The following drugs had no significant effect on the tissue and plasma concentration of H^3-norepinephrine and H^3-normetanephrine: regitine (phentolamine), dichlorisoproternol, TM 10 B, hexamethonium and ouabain. (*Hertting, G., Axelrod, J., and Whitby, L. G.: Effect of Drugs on the Uptake and Metabolism of H^3-Norepinephrine, J. Pharmacol. Exp. Ther. 134: 146 (Nov.) 1961.*)

CATECHOL-AMINE UPTAKE Epinephrine and norepinephrine can be stored in tissues other than those in which they were synthesized. Most of the accumulation is in sympathetic nerve endings, which have a storage capacity considerably greater than their normal catechol-amine content. Quantitative aspects of this uptake suggest that it may play an important role in terminating the actions of exogenous and endogenous catecholamines. (*Strömblad, B. C. R., and Nickerson, M.: Accumulation of Epinephrine and Norepinephrine by Some Rat Tissues, J. Pharmacol. Exp. Ther. 134: 154 (Nov.) 1961.*)

MEPHENTERMINE Mephentermine, in humans with mitral stenosis or chronic pulmonary emphysema, caused bronchodilatation, pulmonary vasodilatation, direct stimulation of the respiratory center, and an increased cardiac output through myocardial stimulation. (*Barrera, F., and others: Cardiovascular-Re-*

spiratory Actions of Mephentermine in Mitral Stenosis and Its Effects on Pulmonary Function in Chronic Pulmonary Emphysema, Circulat. Res. 9: 1185 (Nov.) 1961.)

HALOTHANE The pharmacological evidence of the superiority of halothane to other agents is equivocal. Its main virtues are that it is nonirritating and nonexplosive. It does not upset metabolism as do ether or chloroform nor hepatic function as does chloroform. However, there are three seemingly undesirable actions on the circulation. First, it increases vagal activity, thus tending to cause cardiac inhibition. Secondly, it sensitizes the myocardium to epinephrine and thereby predisposes to ventricular arrhythmias. Lastly, it often lowers the blood pressure. The hypotension of halothane is associated with vasodilatation and need not, except at extremely low levels of blood pressure, cause tissue anoxia. Two safety mechanisms are built into the pharmacological action of halothane on the cardiovascular system. First, this agent does not increase the release of catechol amines from the suprarenal gland as do ether, chloroform, and cyclopropane. Secondly, as cardiac irregularities are less likely when the blood pressure is low, the hypotensive action of halothane protects the patient somewhat against dangerous ventricular arrhythmias. Halothane does not produce abdominal relaxation comparable to that obtainable with ether or chloroform. It is useful rather for operations on the head, neck, extremities, and body surface, particularly when the diathermy apparatus is being used to arrest bleeding. It relaxes the parturient uterus; and therefore its use in operative obstetrics, where there is a risk of postpartum hemorrhage, is dangerous. Halothane passes across the placental barrier to the fetus and depresses its respiratory center signifcantly; and for this reason its administration immediately before delivery may also be undesirable. By contrast it is especially useful in children, who tolerate well depression of sympathetic activity. Halothane can therefore be safely administered to children in relatively large doses, and indeed this drug may be the agent of choice for short pediatric surgical procedures. *(Leading Article—Halothane, Lancet 2: 1129 (Nov. 18) 1961.)*

HALOTHANE AND MUSCULAR RELAXANTS In patients anesthetized with thiopental and nitrous oxide the effect of halothane on muscular relaxants was studied by direct electrical stimulation (twenty times per minute) of the median nerve and registration of the contractions of the middle finger. *d*-Tubocurare, in a single dose of 3 mg., affected muscular contractions very little. After introduction of halothane 1.5 per cent, the height of the contractions remained unchanged. A reinjection of *d*-tubocurare (3 mg.), 25 minutes after the primary injection and 15 minutes after the addition of halothane, caused a pronounced diminution of muscular contractions for 15 minutes. Gallamine iodide (30 mg.), also, caused only a minimal reduction of muscular contractions. During the addition of halothane no change occurred. A second injection of 30 mg. of gallamine, 45 minutes after the initial injection and after 40 minutes of inhalation of halothane, produced an almost complete inhibition for 15 minutes. The injection of 2.5 mg. of decamethonium caused complete inhibition of muscular contractions for 16 minutes. Halothane (1.5 per cent) was administered for 25 minutes and 2.5 mg. of decamethonium were injected 40 minutes after the initial injection. There was no perceptible effect on muscular contraction. Twenty milligrams of succinylcholine inhibited muscular contractions for 3 minutes with complete restoration to the initial height in 6 minutes. After 45 minutes of halothane and 55 minutes after the initial dose, the injection of 20 mg. of succinylcholine showed an identical picture. *(Hanquet, M.: Action de l'halothane sur les inhibiteurs de la transmission neuro-musculaire, Anésth. et Analg. 18: 461 (July–Sept.) 1961.)*

DRUG ABSORPTION The peripheral circulation, the absorbing membrane (capillary wall), connective tissue ground substance, and self-depression of subcutaneous absorption of drugs by endogenously liberated compounds such as histamine and 5-hydroxytryptamine all play a role in the absorption of drugs. Epinephrine delays absorption by constricting the terminal vascular bed in the zone of absorption. The capillary flow is thus markedly