OXYMORPHONE The absence of sedative effects and suppression of coughing, and the low incidence of gastrointestinal disturbance are the primary advantages of oxymorphone. Depression of pulmonary ventilation, the most undesirable effect, may be counteracted with nalorphine. (*Wasmuth, C. E., and Homi, J.: Review of Oxymorphone Hydrochloride Analgesia Employed for General Surgery, Cleveland Clin. Quart. 28: 262 (Oct.) 1961.*)

ANTIDOTES Nalorphine is itself a potent analgesic in man and lacks the addicting potential of the opiates. However, its practical application as an analgesic has been frustrated by cost and the fact that it produces extremely unpleasant side effects, including dysphoria and hallucinatory states. Nalorphine penetrates into the brain much more rapidly and in higher concentrations than morphine and has a more rapid rate of egress. This explains why effects of morphine persist longer than the antagonism afforded by nalorphine. While bemegride is capable of lightening the depth of depression, it does not appear to shorten the duration of coma in patients with severe barbiturate intoxication. Neither do bemegride-treated patients awake with higher blood levels of barbiturates than do controls. The antihistamine diphenhydramine has effected rapid relief of the motor reaction to phenothiazine toxicity. (*Done, A. K.: Clinical Pharmacology of Systemic Antidotes, Clin. Pharmacol. Ther. 2: 750 (Nov.–Dec.) 1961.*)

NARCOTIC ACTION Morphine and certain allied analgetic agents prolong and enhance the positive after-potential of frog sciatic nerve, and these actions are antagonized by levallorphan. These observations led to the suggestion that analgetic agents might act by potentiating residual depression which accompaines the positive after-potential. By studying the dorsal root potentials of cat spinal cord it was found that morphine, methadone, meperidine and nalorphine inhibit the residual negativity which constitutes the fifth dorsal root potential. In the case of morphine, methadone and meperidine this was antagonized by nalorphine. (*Krivoy, W. A., and Huggins, R. A.: Action of Morphine, Methadone, Meperidine and Nalorphine on Dorsal Root Potentials of Cat Spinal Cord, J. Pharmacol. Exp. Ther. 134: 210 (Nov.) 1961.*)

MORPHINE On hypothermized (20° to 22° C.) rabbits, a dose of 1 mg./kg. morphine by intravenous administration does not have a depressant influence on respiration. Likewise, no essential changes were observed in the respiratory function of the blood, rate of blood flow and blood pressure. (*Volynskii, B. G., and Bender, K. I.: Action of Morphine on Respiration and on Haemodynamics in Hypothermia, Farmakol. i Toksikol. 23, 500, 1960.*)

RO 4-1778/1 The respiratory and circulatory effects of RO 4-1778/1 were investigated. One milligram per kilogram was administered intravenously in 36 patients anesthetized with thiopental sodium and nitrous oxide-oxygen. Respiratory depression was produced which was not prevented or antagonized by levallorphan, 0.02 mg./kg. The degree of analgesia produced by 1 mg./kg. was about the same as that produced by meperidine, 0.5 mg./kg.; the duration of effect of RO 4-1778/1 was longer than that of meperidine; and the analgesic action was not accompanied by a significant hypnotic effect. (*Foldes, F. F., Moore, J., and Suna, I. M.: Studies on Respiratory Circulatory, and Analgesic Effects of 1 (P-Chlorophenethyl)-6,7-Dimethoxy-2-Methyl-1,2,3,4-Tetrahydroisoquinoline (RO 4-1778/1), Amer. J. Med. Sci. 242: 282 (Dec.) 1961.*)

A new, nonnarcotic analgesic, RO 4-1778/1, was evaluated in 101 patients with pain due to various causes. Its safety on chronic administration studied in 50 patients who did not require analgesic medication. It was concluded to be an effective analgesic in acute and chronic pain of mild to marked intensity. Nausea is an occasional side effect of larger dosage. It is nonaddictive and has no side effects in daily doses of 240 mg. given over a period of six months. (*Brandman, O.: Clinical Evaluation of Effectiveness and Safety of New Analgesic, Amer. J. Med. Sci. 242: 694 (Dec.) 1961.*)

A double-blind study was carried out with RO 4-1778/1, 60 mg. codeine sulfate, 60 mg. dextro-propoxyphene 65 mg. and a placebo. RO 4-1778/1 was found to be as effective as codeine, milligram for milligram, and free of

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-*