

in *Human and Canine Plasma, J. Lab. & Clin. Med.* 50: 769 (Nov.) 1957.)

### CATECHOLAMINE METABOLISM

Epinephrine, norepinephrine and 3-Hydroxytryptamine were injected intraperitoneally in rats. Chromatographic examination of a 24-hour urine specimen showed that oxymethylation of the phenolic hydroxide (occupying the meta-position of the catechol nucleus with respect to the side chain) had occurred. In addition, a major portion was conjugated with glucuronic acid. Iproniazid increased the percentage of conjugated catecholamine at the expense of the free oxymethylated metabolite. These observations indicate that oxy-methylation of catechol amines occurs prior to oxidative deamination and that this pathway is a principle route of epinephrine and norepinephrine metabolism. Successive replacement of phenolic hydroxyl groups of sympathomimetic amines is known to shift pharmacologic activity from the peripheral to the central nervous system with concomitant loss of pressor action. Many of the physiological actions of epinephrine and norepinephrine may conceivably be mediated through oxy-methylated metabolites. (Axelrod, J., Senoh, S., and Witkop, B.: *O-methylation of Catecholamines in Vivo*, *J. Biol. Chem.* 233: 697 (Sept.) 1958.)

**CATECHOLAMINES** The properties are described of an enzyme that can carry out O-methylation of catecholamines by transferring the methyl group of S-adrenosylmethionine to the hydroxyl group in the metaposition of epinephrine and other catechols. The enzyme is in the soluble fraction of liver and other organs. It requires a divalent cation and is inhibited by sulfhydryl binding reagents. (Axelrod, J., and Tomchick, R.: *Enzymatic O-methylation of Epinephrine and Other Catechols*, *J. Biol. Chem.* 233: 702 (Sept.) 1958.)

**NOREPINEPHRINE** A patient with bulbar paralysis of undetermined etiology required continuous intravenous infusions of norepinephrine in concentrations of 8 to 32 ampules per liter to produce and maintain a systolic blood pressure of 100 mm. of mercury. In spite of the high dosage required for two weeks, the patient eventually made a full re-

covery without renal complications or gangrene of the extremities. (Russell, K. P.: *Selected Obstetrical Conferences from the Los Angeles County Hospital, West. J. Surg.* 66: 240 (July-Aug.) 1958.)

**ETHER** Administration of diethyl ether to patients for operation resulted in a marked increase in the plasma concentration of a substance resembling noradrenalin. The concentration of adrenalin was only slightly increased. Since bilateral adrenalectomy did not cause the elevated plasma concentration of noradrenaline to return to normal, the increased quantities of circulating noradrenalin likely do not originate in the adrenal medulla. (Price, H. L.: *Circulating Adrenaline and Noradrenaline During Diethyl Ether Anesthesia in Man, Clinical Science* 16: 377 (May) 1957.)

**ALDOSTERONE** Normal man is capable of oxygenating corticosterone to aldosterone. Further study is needed to establish whether or not this conversion occurs within the adrenal cortex. (Seltzer, H. S., and Clark, D. A.: *Evidence for Conversion of Corticosterone to Aldosterone in Man, Proc. Soc. Exper. Biol. & Med.* 98: 674 (July) 1958.)

**ADRENAL HORMONES** The cardiac effects, both functional and morphologic, of adrenal hormones were studied in thirty heart-lung preparations. Measurements were made of cardiac output, outflow pressure and the electrocardiogram. In the control series, cardiac work, output, and rate fell slightly and gradually in the course of the 70-minute experiments. No macroscopic or microscopic alterations were observed in the postmortem examination of these hearts. The infusion of epinephrine or norepinephrine resulted in a marked rise in cardiac work and rate which dropped below their control values after cessation of the infusion. Hydrocortisone alone did not cause any significant alteration in function. However, all the hearts receiving one of the adrenal hormones presented extensive lesions of the myocardium, valves, and coronary vessels. The lesions were more severe in the hearts in which both adrenal hormones were used. (Nahas, G. G., and others: *Functional and Morphologic Changes in Heart-Lung*

*Preparations Following Administration of Adrenal Hormones, Am. J. Path. 34: 717 (July-Aug.) 1958.*

**METHOXAMINE REACTION** Since 1952 methoxamine (Vasoxyl) hydrochloride has been successfully employed in the treatment of paroxysmal supraventricular tachycardia when the usual simple measures to stimulate the vagus have failed. The mechanism of action in terminating the tachycardia is believed to be a rise in pressure in the arteries which activate all four afferent pathways concerned with cardiac slowing, viz., the baroreceptors in the carotid sinuses and aortic arch. The usual dose of methoxamine for the therapy is 4–20 mg., undiluted, given by slow intravenous injection. An occasional severe reaction, characterized by excruciating headache, projectile vomiting, general nervousness, and rectal and vesical tenesmus occurs during the administration of the drug. Although such a severe reaction can usually be avoided by slowing or momentarily stopping the injection if the patient complains of a premonitory tingling sensation, nevertheless atropine—which is the physiological antagonist—should be available to counteract serious difficulty. (*Durham, J. R.: Severe Reaction to Methoxamine Hydrochloride, J. A. M. A. 167: 1835 (Aug. 9) 1958.*)

**PROMAZINE IN LABOR** A new method of analgesia and relaxation in labor is afforded by the combination of promazine (Sparine) and meperidine. Promazine 50 mg. is given intravenously to the patient when labor is established (except when delivery is expected within one hour). Subsequently, meperidine 25–50 mg. is administered intravenously and delivery is accomplished under low spinal anesthesia. Promazine is contraindicated in patients with an asthmatic syndrome because (1) marked hypotension develops in such patients given promazine and (2) the nasal and throat congestion produced by the drug may be a reflection of the same processes occurring in the respiratory tract of asthmatic patients. No “clinical hypotension” was encountered when this combination of promazine and spinal anesthesia was employed. Total evaluation of patients showed 57 per cent with excellent and

29 per cent with good results; 85 per cent of the infants were fully alert and 12 per cent were drowsy. (*Wegryn, S. P., and Marks, R. A.: Promazine, Meperidine and Spinal Anesthesia for Labor and Delivery, J. A. M. A. 167: 1918 (Aug. 16) 1958.*)

**CHLORPROMAZINE JAUNDICE** Small doses (50 mg.) of chlorpromazine may quickly produce a severe jaundice, which may be extremely difficult to differentiate from jaundice of more common origin. When biliary tract disease is known or suspected, extreme caution in the use of this drug is imperative. (*Malabed, L. L., and Carlson, E.: Chlorpromazine Versus Surgical Jaundice, West. J. Surg. 66: 228 (July-Aug.) 1958.*)

**PROTAMINE** Protamine sulphate in low concentrations affects rate and yield of blood thromboplastin, but has no effect on formed thromboplastin. Higher concentrations inhibit a reaction between blood thromboplastin, prothrombin and calcium. (*Hougie, C.: Anticoagulant Action of Protamine Sulphate, Proc. Soc. Exper. Biol. & Med. 98: 130 (May) 1958.*)

**MORPHINE METABOLISM** The kinetics of the enzyme actions found in a mouse liver microsome system responsible for demethylation of morphine and similar compounds has been studied. The system responsible for demethylation of narcotic compounds differs from that for demethylation of aminoazo dyes. The similarity between the receptors for narcotic action of morphine and allied compounds and the receptors for the enzymes that demethylate these compounds is not as great as has been proposed. (*Takemori, A. E., and Mannering, G. J.: Metabolic N- and O-Demethylation of Morphine- and Morphinan-Type Analgesics, J. Pharmacol. & Exper. Therap. 123: 171 (July) 1958.*)

**FLUOTHANE** Cardiovascular complications during Fluothane administration were found to be minimal when low concentrations (0.8 to 1.0 per cent) were not exceeded for maintenance. Supplemental meperidine, thio-pentone, and relaxants were used when deeper planes of anesthesia or relaxation were re-