of myocardium destroyed by previous infarction. The long-term surgical results and the effect on the natural history of disease remain to be determined.

In their discussion of the medical and surgical treatment of dissecting aneurysm, R. DeSanctis and M. Buckley emphasized the advantages of the Wheat–Palmer medical management concept. The aims of therapy are to reduce systolic blood pressure to 100–120 torr and concurrently to reduce the velocity of ventricular contraction. To achieve this, they utilize trimethaphan, reserpine, propranolol, methyldopa, chlorothiazide, and sedation, as needed. They report a 50 per cent overall survival rate when the aneurysm is treated medically. The major complication of therapy is hypotension. Aneurysms (of the distal aorta) are frequently treated surgically. From an anesthetic point of view, the major problem occurs postoperatively, when interstitial edema may develop in the lung compressed during thoracic aneurysm repair. Dr. Buckley believes that an increasing A-aD_{O_2} is a prime indication for steroid therapy; he uses 1–2 g methylprednisolone every six hours.

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Drugs and Their Actions

ROUTE OF ADMINISTRATION AND EFFECTIVENESS OF PROPRANOLOL Certain unpredicted disparities between the β-adrenergic blocking effects of propranolol given by different routes have been described. For a given plasma concentration, the effect is greater 2 hours after oral administration than after iv administration. A metabolite with beta-blocking properties, 4-hydroxypropranolol, is detectable in blood after oral but not after iv administration. The authors have tried to clarify these disparities by using the principles of bioassay to study the relationship between the effects of a drug and its plasma concentrations. The effects of propranolol in five young adults were measured by a standardized test of isoproterenol sensitivity. The iv dose of isoproterenol necessary to increase the resting heart rate by 25 beats/min (*i.e.*, chronotropic dose = CD_{25}) was determined before and 15 minutes, three hours, and six hours after iv injection of 20 mg propranolol. CD_{25} was also determined for each of five consecutive days before and two and six hours after oral administration of two single doses of 20 to 80 mg of propanolol, the second dose being double the first. One of these single doses was selected for the long-term study and given every six hours. CD_{25} was measured two and six hours after the twenty-first dose on the sixth day. Plasma samples after each test were assayed fluorometrically for propranolol only, not for the metabolite. Two hours after oral administration of single dose of propranolol, the degree of beta blockade associated with a given plasma propranolol concentration was greater than that seen with the same concentration achieved iv. This disparity was no longer present after six hours. Following long-term oral administration, the β-blocking effects of similar plasma levels were not different from those achieved following iv administration. This is explained by the formation after single oral doses of the active metabolite, 4-hydroxypropranolol, which has a shorter half-life than propranolol. The metabolite is not produced after iv administration of single doses. At the end of a six-hour dosage interval and after chronic oral administration, the effects of propranolol could be attributed entirely to the plasma levels of the parent drug. (*Cleveland, C. R., and Shand, D. G.: Effect of Route of Administration on the Relationship β-Adrenergic Blockade and Plasma Propranolol Level, Clin. Pharmacol. Therap. 13: 181–185, 1972.*)