tassium depletion, and, with large doses, possibly red cell hemolysis.

Effects of Local Anesthetic Agents on Heart Force. W. P. ROGERS, M.D., D. M. STEWART, M.D., J. E. MAHAFFEY, M.D., E. F. WOODS, PH.D., and S. M. WITHERSPOON, M.D., *Departments of Anesthesiology and Pharmacology, Medical College of South Carolina, Charleston, South Carolina.* Six local anesthetic agents: Procaine, cocaine, lidocaine, chloroprocaine, tetracaine, and hexylcaine were assessed for their relative potency in depressing myocardial contractile force (MCF) in dogs. For each animal the cardiovascular response to procaine, 60 mg./kg. intravenously, as well as the response to one or more of the other agents, was determined. This permits calculation of potency of the other agents relative to procaine. *Method:* The HCl salts of the drugs were administered intravenously over a 2-minute period to "open chest" dogs anesthetized with 25 mg./kg. of pentobarbital and ventilated artificially with room air. A Walton-Brodie strain gauge arch was sutured to the right ventricle for direct recording of MCF. Aortic BP, heart rate, and ECG lead 2 are also recorded. In some experiments aortic blood flow, as an index of cardiac output, was recorded using a square-wave electromagnetic flowmeter. *Results:* Sixty-four experiments on 30 animals have been completed. Two animals died following injection, one of ventricular fibrillation after procaine, and a second of asystole following tetracaine. Responses to injection of different agents have been qualitatively similar in the several parameters. Each injection of drug is followed by coincident decrease of MCF, systolic and diastolic blood pressure, heart rate and aortic blood flow and by the development of ECG changes suggesting intraventricular conduction block. Typical tracings showed the following sequence with general parallelism in all parameters: (1) Initial depression appearing at 20 to 90 seconds and reaching a nadir at 3 to 8 minutes after beginning injection. (2) Either temporary stabilization at the low level or a temporary rise to or above control level. This occupies 2 to 5 minutes. (3) A slow decline to or slightly below the immediate postinjection level over 20 to 30 minutes. (4) A gradual return to control over 20 to 70 minutes. By preliminary experiments, doses of the different drugs to provide roughly similar levels of depression were established so that any compensatory neurohumoral effects would be similar for the different drugs. Mean blood pressure depression ranged from 36 per cent with chloroprocaine to 42 per cent with procaine. The blood pressure response to cocaine has been unpredictable, 2 of 5 animals exhibiting elevation during the period of maximal heart force depression. This has not occurred with any other drug. Depression of aortic blood flow measured in 25 experiments ranged from 32 per cent for lidocaine and procaine to 44 per cent for chloroprocaine. Depressions of MCF were computed as percentage decrease per mg./kg. of drug injected. For each animal the potency of the drug or drugs injected was determined relative to procaine, which was assigned a potency of 1.0 as a depressant of MCF. The means of these individual determinations expressed as relative potency are: procaine–1.0, chloroprocaine–2.2, hexylcaine–4.6, lidocaine–5.25, cocaine–6.6, tetracaine–8.3. [Supported by grants from the National Heart Institute and the Rock Hill, South Carolina, United Fund.]

Effects of Neostigmine on Isolated Human Muscle. PHIROZE B. SABAWALA, M.D., and JOHN B. DILLON, M.D., *Department of Surgery/Anesthesiology, University of California Medical Center, Los Angeles, California.* Most, if not all, effects produced by a potent anticholinesterase such as neostigmine can be explained on the basis of cholinesterase inhibition at the neuromuscular junction. However, there is equally good evidence that aside from its powerful anticholinesterase activity, neostigmine also acts directly on the muscle membrane in some unknown manner (Riker, W. F., and Wescoe, W. C.: J. Pharmacol. Exp. Ther. *88:* 58, 1946). By adding increasing amounts of neostigmine to the physiologic saline bathing an isolated nerve-muscle preparation, the various effects of this drug can easily be demonstrated. These effects can conveniently be described as: (1) anticurare effect, (2) positive inotropic effect, (3) spontaneous twitching and (4) two phase