Literature Briefs

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Briefs were submitted by Drs. J. Adriani, C. M. Ballinger, R. B. Boettner, R. Bickwell, P. P. Bosomworth, D. R. Buechel, M. T. Clarke, D. Duncalf, J. E. Eckenhoff, N. Greene, M. Helrich, G. Hohmann, J. Jacoby, E. M. Kavan, H. Linde, F. C. McPartland, W. H. Mannheimer, J. W. Pender, R. E. Ponath, A. D. Randall, H. S. Roe, E. W. Robinson, L. J. Saidman, P. H. Sechzer, and E. A. Talmage. Briefs appearing elsewhere in this issue are part of this column. Abstracts of Russian and Japanese literature were obtained from Excerpta Medica Foundation.

ARRHYTHMIAS It has been known since 1958 that adrenergic blockade of the heart by surgical or chemical (drug) means can modify digitalis induced ventricular arrhythmias. Dichlorisoproterenol (DCI) was the first beta-adrenergic blocking agent studied for this purpose. It effectively reversed ventricular arrhythmias but, because of potent sympathomimetic side effects, it has not been used clinically. Pronethalol and other beta blocking agents without sympathomimetic effects have been found to have anti-arrhythmic properties. The mechanism for this anti-arrhythmic effect may not be in the beta blocking properties of the agents. Digitalis is known to cause an efflux of potassium from the myocardial cells which may lead to ventricular arrhythmias. Quinidine, procaine amide and pronethalol reduce potassium loss in dogs and may stabilize the heart by this mechanism. The anti-arrhythmiac effect of pronethalol was studied in 24 dogs (5 dogs pretreated with reserpine, 5 with guanethidine and 6 with promethalol). Pretreatment with any of these agents did not prevent the appearance of ventricular arrhythmias when the dogs were challenged with acethylstrophanthidin. The arrhythmias were effectively reversed in all the animals with pronethalol. However, the dosage necessary to reverse the arrhythmias, 2.5 mg./kg., was about ten times that which produced effective beta-adrenergic blockade as established by response to tyramine. Subsequent work has shown that the dextro-isomer of pronethalol was equally effective as the levo-isomer used in this study in reversing digitalis induced arrhythmias although it has only one-fortieth the beta-adrenergic activity of the levo-isomer. (*Arocsty, J. M., and Cohen, J.: The Effects of a Beta-Adrenergic Blocking Agent Pronethalol on Digitalis Induced Ventricular Arrhythmias, Amer. Heart J. 71: 503 (April) 1966.*)

REVIEWER'S COMMENT: Other work (*Benfey and Varma: Brit. J. Pharmacol. 26: 3, 1966*) confirms the impression that the antifibrillatory action of pronethalol and propranolol (a beta blocker 10 times as potent as pronethalol) is due to properties not directly related to beta-blockade.

CARDIOVERSION A significantly greater number of patients in whom the pre cardioversion ECG reflects digitalis overdosage will manifest post cardioversion ventricular arrhythmias. The proposed mechanism for the above is that the electrical shock affects myocardial membranes resulting in a loss of intracellular potassium. When a critical loss has occurred, toxic effects of the cardiac bound glycoside ensue. To decrease the risk attending cardioversion it is recommended that: (a) digoxin be discontinued for 24 hours prior to cardioversion; (b) longer acting drugs be discontinued for two days; (c) cardioversion be postponed if the pre cardioversion ECG shows signs of digitalis toxicity or if hypokalemia is present; (d) the least energy needed for cardioversion be employed by starting with 25–50 watt seconds. If serious ectopic ventricular beats are encountered, they may be abolished by intravenous lidocaine 50 mg., procaine amide 100 mg., diphenyl hydantoin 100 mg.,

or propanolol 5 mg. (*Kleiger, R., and others: Cardioversion and Digitalis, Circulation 33: 878 (June) 1966.*)

CARDIOVERSION Precordial direct current shock for the reversion of atrial fibrillation to sinus rhythm was applied to 27 patients with heart disease. Cardiodynamic studies were performed 24 hours before and 24 hours after precordial shock. Six patients who failed to revert constituted a control group and showed no significant changes in cardiac function after precordial shock. In ten patients with mitral valve disease, mean cardiac index increased from 1.99 liters/min./m.^{2} in atrial fibrillation to 2.63 liters/min./m.^{2} in sinus rhythm. Resting mean oxygen consumptions were similar but heart rate were slightly higher in sinus rhythm. Resting stroke volume increased from 57 ml./beat to 65 ml./beat. Peripheral vascular resistance varied inversely with cardiac output while arterial pressure remained remarkably constant. Arteriovenous blood oxygen differences fell from 6.71 ml./100 ml. during fibrillation to 4.72 ml./100 ml. in sinus rhythm. In four patients with dominant aortic stenosis or insufficiency, mean oxygen consumption and heart rate were similar in the two rhythms. Cardiac index increased from 1.76 before to 2.41 liters/min./m.^{2} after reversion. Stroke volume was greater and peripheral vascular resistance fell as blood flow increased in sinus rhythm. Arteriovenous blood oxygen differences fell from 8.29 ml./100 ml. to 6.02 ml./100 ml. in sinus rhythm. Six patients with chronic arterial fibrillation, small hearts, no murmurs, and no evidence of heart failure or ischemic heart disease were termed benign fibrillators. Average values for oxygen consumption, A-V oxygen difference, heart rate, cardiac index, and stroke volume for this group were not significantly different before and after reversion. Data obtained during exercise were essentially similar in the control patients before and after precordial shock. In the group with mitral valve disease, mean cardiac index during exercise increased from 2.74 liters/min./m.^{2} in atrial fibrillation to 3.34 liters/min./m.^{2} in sinus rhythm. Mean A-V oxygen difference fell from 10.16 to 8.48 ml./100 ml. in this group. The increased cardiac output during exercise reflected the higher resting level, since the changes induced by the exercise were similar in the two rhythms. Reversion from atrial fibrillation to sinus rhythm with precordial shock in the absence of myocardial depressants or changes in drug therapy produces a significant improvement in cardiac output due to an increased stroke volume in patients with valvular disease. In patients with benign fibrillation reversion from atrial fibrillation is not associated with improvement in cardiac output or stroke volume. Exercise heart rates are similar before and after reversion in valvular heart disease but lower in benign fibrillation. After reversion, the increment in heart rate induced by exercise is significantly reduced in patients with valvular heart disease and benign fibrillation. (*Killip, T., and Baer, R. A.: Hemodynamic Effects after Reversion from Atrial Fibrillation to Sinus Rhythm by Precordial Shock, J. Clin. Invest. 45: 658 (May) 1966.*)

CARDIAC INNERVATION Electrical stimulation of various sites in the central nervous systems of experimental animals and central nervous system lesions in man can produce changes in the electrocardiogram in the absence of demonstrable heart disease. The effects on the electrocardiogram of section and stimulation of the right and left stellate ganglia were studied in dogs. Right stellate ganglionectomy or left stellate stimulation produced a prolonged Q-T interval and increased T-wave amplitude. Left stellate ganglionectomy or right stellate stimulation produced increased T-wave negativity without measurable changes in the Q-T interval. The left stellate predominantly influences the anterior ventricular walls. The changes in sympathetic tone could be correlated with changes in the ventricular refractory period, *i.e.*, stimulation of the right ganglion or ablation of the left ganglion prolonged the refractory period of the posterior ventricular surface causing an increased Q-T interval and T-wave changes. The electrocardiographic changes produced here are similar to those in patients with CNS disease, suggesting that alterations in sympathetic tone may account for these changes. (*Yanowitz, F., Preston, J. B., and Abildskov,*