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MB Isoenzyme of Creatine Phosphokinase and Exercise Stress Tests

To the Editor:

The article by Marmor et al1 entitled "MB isoenzyme of Creatine Phosphokinase: Indicator of Ischemia in Coronary Arterial Disease" once again calls attention to the difficulty of interpreting an elevated concentration of the MB isoenzyme of creatine phosphokinase following an abnormal exercise stress test in the presence of normal levels of myoglobin and total creatine phosphokinase in the serum and in the absence of diagnostic electrocardiographic changes. Marmor et al indicated that "in severe hypoxia, metabolic changes occur in the membrane of the myocardial cell, changes which are responsible for the release of the MB isoenzyme of creatine phosphokinase."2 These investigators concluded that the patient had severe hypoxia, and supporting laboratory data "ruled out acute myocardial infarction."3

An equally tenable argument might be that the patient suffered a small myocardial infarction. Exercise-induced myocardial ischemia was not associated with an increase in the MB isoenzyme of creatine phosphokinase, as measured by a very sensitive method, in our laboratory.2 In another report,4 neither catecholamine stimulation nor atrial pacing to angina resulted in release of enzyme from the heart. In our laboratory, atrial pacing to angina did not result in an increase in the level of the MB isoenzyme of creatine phosphokinase either in the coronary sinus or systemic circulation. Thus, it seems very unlikely that myocardial ischemia would result in an elevation of the concentration of the isoenzyme of creatine phosphokinase. On the other hand, the MB isoenzyme of creatine phosphokinase is very sensitive, and an increase in the level may reflect acute myocardial infarction even in the presence of a normal level of total creatine phosphokinase.4 This determination of the level of the isoenzyme is considerably more sensitive to the presence of myocardial necrosis than are serum levels of myoglobin or diagnostic electrocardiographic changes. When properly measured, the level of the MB isoenzyme of creatine phosphokinase may be the most sensitive method currently avail-

<table>
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Table 1—Levels of Enzymes in 42-Year-Old Man after Direct-Current Shock

FIGURE 1. Exercise ECG from 42-year-old man.
able for the detection of acute myocardial necrosis.\textsuperscript{6}

A 42-year-old man with severe three-vessel and left main coronary artery disease developed pain in the chest and ST-segment depression during an exercise test in our laboratory. Immediately following exercise, he developed ventricular tachycardia and then ventricular fibrillation, which was converted with direct-current shock. Subsequent enzymatic analysis (Table 1) and serial electrocardiograms (Fig 1) indicated the absence of myocardial infarction. Thus, this level of myocardial hypoxia, ventricular fibrillation, and direct-current shock did not result in elevation of the concentration of the MB isoenzyme of creatine phosphokinase in this patient.

Therefore, an elevation of the concentration of the MB isoenzyme of creatine phosphokinase following exercise-induced myocardial ischemia is much more likely to be a result of myocardial infarction than myocardial hypoxia.

\textbf{Frederick L. Gobel, M.D.}
\textbf{and Richard R. Nelson, M.D.}
\textbf{Minneapolis}

\textit{Reprint requests: Dr. Gobel, 2545 Chicago Avenue, Suite 402, Minneapolis 55404}

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\textbf{Unusual Hepatocellular and Cardiovascular Complications of Disopyramide}

\textit{To the Editor:}

Recent publications in Chest have reported the efficacy of intravenous disopyramide phosphate in the treatment of ventricular and supraventricular tachyarrhythmias.\textsuperscript{1,2} Reported side-effects have been related principally to anticholinergic properties of the drug or occasional systemic hypotension. In our own series of 50 patients, we have similarly found intravenous disopyramide a valuable antiarrhythmic agent, but in five patients, have encountered complications which have not previously been discussed.

\textbf{CASE REPORTS}

\textbf{CASE 1}

A 74-year-old man presented with paroxysmal ventricular tachycardia. His arrhythmias were controlled by administration of intravenous disopyramide 2.0 mg/kg followed by 0.2 mg/kg/hour. A mild fall in arterial pressure from 120/90 to 95/75 mm Hg resulted. However, after five hours, the infusion was discontinued, and disopyramide 150 mg po, qid commenced with prompt return of his arterial pressure to pre-existing levels within two hours. Three days later, abnormal results of liver function tests were noted. Serum alanine-amino-transferase peaked on the fourth day after disopyramide was commenced at 6,200 U/L (normal < 35). Serum alkaline phosphatase rose to 125 U/L (normal 25-100), serum bilirubin to 88 µmol/L (normal < 20) and prothrombin ratio was prolonged to 2.8 (therapeutic range 2.0-3.5). At the time of deterioration in hepatic function, Swan-Ganz catheterization showed a pulmonary capillary wedge pressure of 20 mm Hg and normal right atrial pressures. Urine output and renal function were maintained and, although disopyramide may cause significant myocardial depression, the findings appeared to reasonably exclude either low cardiac output or congestive cardiac failure as the cause of the hepatic deterioration. He was receiving no known hepatotoxic agents, and neither hepatitis antigen nor catheteritis was detected. Complete reversal in his biochemical abnormalities over 14 days after disopyramide was ceased, strongly suggested drug hepatotoxicity. Liver biopsy done six days after cessation of disopyramide showed nonspecific inflammatory changes, with no intrahepatic cholestasis which has been reported as a rare toxic effect of the drug.\textsuperscript{3}

\textbf{CASE 2}

A 55-year-old man with ischemic heart disease and refractory ventricular tachycardia was referred for electrophysiologic study. Prior to study, all medications were curtailed for five days. During sinus rhythm with left bundle branch block and PR interval 200 msec, his HV interval was prolonged (80 msec). Ventricular tachycardia was induced by programmed ventricular extrastimuli. This could not be terminated by pacing techniques. Disopyramide 100 mg IV was administered and his tachycardia then terminated by rapid right ventricular pacing. In sinus rhythm, immediately post-reversion, the HV interval was 80 msec. He then developed 2:1 and complete infra-Hisian block, persisting until 1:1 AV conduction resumed 20 minutes later. The abnormal HV prolongation following disopyramide and the period of 2:1 AV block suggested that disopyramide and not catheter-induced right bundle branch block was the cause of complete heart block. Although disopyramide is reportedly safe,\textsuperscript{4} we feel that caution is necessary when it is administered to patients with impaired distal conduction.

\textbf{CASES 3-5}

Although the more frequent effect of disopyramide was mild systemic hypotension, three of the 50 patients demonstrated a hypertensive response. Both systolic and diastolic arterial pressures rose by 40-50 mm Hg and fell to pre-existing levels within two to three hours of cessation of disopyramide. The evidence is circumstantial, but is consistent with demonstrated peripheral vasconstrictor effects of the drug.\textsuperscript{5}

\textbf{Andrew M. Tonkin, M.D.}
\textbf{Sandra E. Joel, B.Pharm.}
\textbf{Julie L. Reynolds, B. Pharm.}
\textbf{Bedford Park, South Australia}

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