The Natural History of Conduction System Disease in Myotonic Muscular Dystrophy as Determined by Serial Electrophysiologic Studies

ERIC N. PRYSTOWSKY, M.D., EDWARD L. C. PRITCHETT, M.D., ALLEN D. ROSES, M.D., and JOHN GALLAGHER, M.D.

SUMMARY To evaluate the progression of conduction system disease in myotonic muscular dystrophy, nine patients underwent serial electrophysiologic studies at a mean of 35 months apart. At the initial study, seven patients had first-degree atrioventricular block and three of these seven had disease in the His-Purkinje system (HV > 55 msec). At the second study, seven patients had prolonged HV intervals, and during the almost 3-year period, HV intervals increased by at least 5 msec in all seven patients. No electrophysiologic or electrocardiographic measures could be found that correlated with progression of conduction disease in these patients. Because of the failure of electrophysiologic measures to predict progression of conduction disease in these patients, electrophysiologic studies are recommended only for symptomatic patients. If significant disease is found in either impulse formation or conduction, permanent pacemaker therapy is warranted.

MYOTONIC MUSCULAR DYSTROPHY (Steinert’s disease, dystrophia myotonica, myotonica atrophica), a genetic disease, affects many organ systems.1-5 Cardiac involvement is frequent and is most commonly manifest as conduction disturbances, although arrhythmias may also occur.1-21 Previous studies using His bundle electrocardiography have located the conduction disturbances in the His-Purkinje system in most patients.5-9, 13, 14 Because prolonged conduction in the His-Purkinje system has been recognized as an early sign of developing complete atrioventricular block,22, 23 its significance in patients with myotonic muscular dystrophy should be studied. Sudden death is relatively common in this group of patients,1-3, 5, 6, 10, 12, 13, 17, 19, 20 and may be related to progressive conduction system disease underlying the His-Purkinje changes. We evaluated progression of conduction system disease by performing serial electrophysiologic studies in patients with myotonic muscular dystrophy.

Methods

Nine patients with myotonic muscular dystrophy who had undergone electrophysiologic study between February 1974 and June 1976 were studied again between January–March 1978. Patients were selected for restudy if at least 18 months had elapsed between the first study and January 1978. Each patient had overt muscular disease and was being followed in the Duke Neuromuscular Research Clinic. The diagnosis of myotonic muscular dystrophy had been made by Allen D. Roses.1, 2

Informed consent was obtained from each patient before study in the Clinical Electrophysiology Laboratory of Duke University Medical Center. All patients were studied in the postabsorptive, nonsedated state. His bundle electrograms were obtained with a tripolar catheter (USCI) introduced percutaneously via the right femoral vein.24 A quadrupolar catheter (USCI) was positioned in the right ventricle to determine if ventriculoatrial conduction was present. A second quadrupolar catheter (USCI) was positioned in the lateral right atrium in all patients in whom ventriculoatrial conduction was confirmed.

The conduction system was assessed during sinus rhythm and with stimulation using fixed-rate pacing and the extrastimulus technique25 in eight patients. Only a His bundle electrogram was obtained in patient 3. Pacing was done with a special stimulator (built by Jackie Kasell, Department of Medicine, Duke University), applying the least amount of energy needed to capture the heart consistently.

Data were recorded on tape at 3/4 inch/sec (Ampex PR2200) and simultaneously written out at 200 mm/sec (Siemens-Elema mingograf 1605). In addition to intracardiac recordings, simultaneous electrocardiographic leads I, II, III and V, were obtained. The results from the initial and final study were compared by means of linear regression analysis.

Results

Nine patients had a repeat electrophysiologic study a mean of 35 months (range 19-48 months) after their initial study (table 1). At the time of the study, no patient was taking any medicine known to affect intraventricular or infranodal conduction. The HV interval was prolonged (>55 msec) in three patients at the initial study and in seven patients at the final study (table 2, fig. 1). Of the nine patients, only the two with a normal

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Table 1. Patient Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Interval between studies (months)</th>
<th>Cardiovascular symptoms</th>
<th>Therapy</th>
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<td></td>
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<td></td>
<td>I</td>
<td>F</td>
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<td>36</td>
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</table>

Abbreviations: I = initial study; F = final study; N = none; PP = permanent pacemaker; PS = presyncope.

PR interval had a normal HV interval at the final study; five had a 5–10-msec increase and two had a >10-msec increase in the HV interval between studies (fig. 1).

In the eight patients in whom it could be obtained, the AH interval was normal at the initial study. At the final study, the AH interval was consistently abnormal in patient 3 and was intermittently abnormal in patient 9.

Electrocardiographic Correlations with His Bundle Recordings

Seven patients had first-degree atrioventricular block at the initial study (table 2). Between studies, a marked increment in the PR interval was noted only in patient 3. Four patients had an intraventricular conduction delay at the initial study, and only one had an associated normal PR interval. There was no change in the QRS morphology or QRS interval in any patient between studies (table 2).

Table 2. Conduction Intervals (msec)

<table>
<thead>
<tr>
<th>Sinus cycle length</th>
<th>PR</th>
<th>QRS</th>
<th>AH</th>
<th>HV</th>
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<td>Pt</td>
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<td>F</td>
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<td>—</td>
<td>1010</td>
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<tr>
<td>9</td>
<td>730</td>
<td>780</td>
<td>220</td>
<td>220</td>
</tr>
</tbody>
</table>

*In atrial fibrillation at time of initial study.
†PR interval from ECG 8 months before initial study.

Abbreviations: I = initial study; F = final study; LBBB = left bundle branch block.
As it would be desirable to have a noninvasive method to detect changes in the HV interval, we attempted to correlate conduction intervals on the ECG with those obtained by means of the His bundle catheter. There was no correlation between: 1) first-degree atrioventricular block and HV interval at the initial study, 2) the increase over time in HV and PR interval, or 3) the increase over time in HV and QRS interval. In addition, there was no relationship between the value of the initial HV interval and the degree to which it progressed (fig. 1). In fact, the largest increases in HV interval were seen in patients 3 and 6, both of whom had a normal initial HV interval. Finally, there was no correlation between the increase in HV interval and either the age of the patient or the interval between studies.

### Functional Properties of the Atrioventricular Conduction System

The results from atrial and ventricular pacing are shown in table 3. During incremental fixed-rate atrial pacing, all eight patients tested had normal responses in the initial study, i.e., 1:1 atrioventricular conduction at pacing cycle lengths <460 msec (130 beats/min). During the final study, two patients had a large increase in the shortest atrial pacing cycle length sustaining 1:1 atrioventricular conduction (fig. 2), but only patient 2 had an abnormal response. In neither study did any patient develop bundle branch block during pacing.

The effective and functional refractory periods of the atrioventricular node were compared between studies (table 3). Although there appeared to be a trend toward an increase in refractoriness of the atrioventricular node between studies, this relationship was not consistent at all cycle lengths tested and the sample sizes in each group were not large enough for meaningful statistical analysis.

### Cardiovascular Symptoms and Pacemaker Therapy

Only patient 5 had cardiovascular symptoms before her initial study (table 1). Several periods of ambulatory monitoring and an analysis of sinus node recovery time at several pacing cycle lengths did not uncover a cause for these symptoms. Because of her symptoms and prolonged HV interval, she was treated with a permanent transvenous pacemaker and was asymptomatic at the second study.

Patient 8 was asymptomatic at his first study, which revealed an HV interval of 75 msec (table 2). Because of the marked prolongation of the HV interval, a permanent transvenous pacemaker was inserted. Although his ECG was unchanged between studies, he had progressive His-Purkinje conduction disease, as evidenced by a 10-msec increase in the HV interval. No patient had cardiovascular symptoms at the final electrophysiologic study.

### Comparison of Progression of Conduction System Disease with Muscular Dystrophy

The patients had little or no progression of their neurological symptoms and signs during this study.
Two of the patients complained that daily activities were becoming more difficult, and had objective evidence of being slightly weaker at the second study; but neither this documented progression of dystrophy during the study period nor the generalized abnormalities present in each myotonic dystrophy patient correlated with the electrophysiologic findings.

**Discussion**

Patients with myotonic muscular dystrophy have a higher incidence of sudden death than the general population.\(^1\) As conduction disturbances are common in these patients, the cause of sudden death may be complete atrioventricular block terminating in either asystole or ventricular fibrillation or both. Therefore, it is important to identify any electrocardiographic or electrophysiologic measures that would predict progressive impairment of the atrioventricular conduction system. Repeat electrophysiologic studies a mean of 35 months after the first study allowed assessment of several parameters that might be predictive.

The most important finding in this study was that the initial HV interval did not predict whether conduction system disease would develop or progress. Between studies, the HV interval increased in seven

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**Figure 2.** Change between studies in the shortest atrial pacing cycle length in which 1:1 atrioventricular (AV) conduction occurred. No patient had an abnormal response at the initial study and only one patient had an abnormal response at the final study.
patients. Although one might expect that the largest increases in HV interval would occur in patients with His-Purkinje disease, this was not the case. Instead, the largest increases in HV conduction time (22 and 20 msec) occurred in patients 3 and 6, who had normal HV intervals at the initial study. The one markedly abnormal HV interval (in patient 8) rose only 10 msec between studies.

We also evaluated noninvasive measures that could predict progression of atrioventricular conduction disease. No electrocardiographic or clinical data correlated with either the presence of His-Purkinje disease or progression of conduction disease, as established by electrophysiologic studies; nor did the severity or progression of the noncardiac manifestations of myotonic muscular dystrophy correlate with the cardiac manifestations.

Clinical Implications

This study confirms that patients with myotonic muscular dystrophy are prone to disease in the His-Purkinje system;13, 14 Moreover, this conduction disturbance becomes progressively worse. The results from one recent study24 suggest that other disorders of the cardiovascular system may be associated with progressive disease in the His-Purkinje system that does not follow a predictable course.

We do not recommend electrophysiologic study of asymptomatic patients with myotonic muscular dystrophy regardless of whether electrocardiographic abnormalities are present. However, patients with a history of syncope or presyncope that is undiagnosed after neurologic and cardiovascular examination, including long-term ambulatory monitoring, should have an electrophysiologic study to evaluate impulse formation and conduction. If significant disease of the sinus node or His-Purkinje system is found, permanent pacemaker insertion is warranted.

Acknowledgment

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