The Billowing Mitral Valve Leaflet
Report on Fourteen Patients

By Neville Bittar, M.D., and Julio A. Sosa, M.D.

SUMMARY
Fourteen patients with billowing mitral valves have been studied. In 11 the abnormality was not accompanied by significant cardiac disability. In three, severe mitral insufficiency required mitral valve replacement. Pathological examination of the excised mitral valves showed myxomatous degeneration of mitral valve substance and chordae tendineae. Inhalation of amyl nitrite by the nine patients with late systolic murmurs resulted in a change from late systolic to pansystolic murmur in seven and to mid-systolic murmur in two. On the basis of the known effects of amyl nitrate, this response gives support to the concept that the critical pathogenetic factor is the degree of elongation of chordae tendineae.

Additional Indexing Words: Marfan's syndrome Mural cusp Amuscular mitral valve leaflets

STUDIES OF PATIENTS with late systolic murmurs have revealed that what was once considered an innocent cardiac murmur is not innocent, but caused by mitral valve insufficiency.1-5 This condition is characterized by the presence of huge leaflets which appear to have partially prolapsed into the left atrium. The present paper attempts to describe this lesion in 14 patients who, while having identical mitral valve deformity, showed wide variation in valvular dysfunction.

Clinical Information
The 14 patients were 16 to 57 years of age, seven of whom were women.

One patient had the typical appearance of Marfan's syndrome, while six others were tall and thin. One woman had Turner's syndrome, a diagnosis established by chromosomal analysis. The external physical characteristics of the remaining six patients were unremarkable.

None of the patients had a history of rheumatic fever or endocarditis. In three, the existence of a cardiac murmur was first detected before the age of 10, and in eight others, after the age of 25 years.

Three patients were asymptomatic, while eight others had mild exertional dyspnea and occasional palpitations. The remaining three showed moderate exertional dyspnea, easy fatigability, and paroxysmal nocturnal dyspnea.

The main findings in these 14 patients are summarized in table 1. Of the two patients without evidence of mitral insufficiency, one (R. B.) had a loud diastolic blow, diagnostic of aortic insufficiency. The other patient (A. G.) who was free of murmurs at the time of catheterization, had a precordial honk at an earlier examination. The systolic murmur, which was best heard at the cardiac apex, was accompanied by a palpable thrill in four patients. The murmur was late systolic in nine patients, and initiated by a click in
Table 1

Clinical Features of 14 Patients with the Billowing Mitral Valve Leaflet

<table>
<thead>
<tr>
<th>Name</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.B.</td>
<td>34</td>
<td>♂</td>
<td>33 Palpitations, dyspnea</td>
<td>Thin, tall, span greater than height; grade III/VI diastolic blow along left sternal border</td>
</tr>
<tr>
<td>A.G.</td>
<td>16</td>
<td>♀</td>
<td>8 None</td>
<td>Thin, tall, slight pectus carinatum; no murmurs detected; precordial honk heard by referring physician</td>
</tr>
<tr>
<td>P.H.</td>
<td>32</td>
<td>♀</td>
<td>31 Occasional palpitations, increasing tiredness</td>
<td>Thin with hyperextensible joints; grade III/VI late systolic murmur</td>
</tr>
<tr>
<td>M.D.</td>
<td>21</td>
<td>♀</td>
<td>6 Palpitations, dyspnea on moderate exertion</td>
<td>Typical Marfan's syndrome; grade IV/VI, late systolic murmur</td>
</tr>
<tr>
<td>T.C.</td>
<td>40</td>
<td>♀</td>
<td>37 Dyspnea on exertion</td>
<td>Short stature, short neck, shieldlike chest, typical Turner's syndrome; grade III/VI, late systolic murmur introduced by click; apical systolic thrill</td>
</tr>
<tr>
<td>J.M.</td>
<td>42</td>
<td>♂</td>
<td>32 None</td>
<td>Unremarkable body habitus; apical systolic thrill; grade IV/VI, late systolic murmur, initiated by click</td>
</tr>
<tr>
<td>D.S.</td>
<td>37</td>
<td>♀</td>
<td>18 None</td>
<td>Tall, thin, span greater than height; apical systolic thrill; grade III/VI late systolic murmur</td>
</tr>
<tr>
<td>D.R.</td>
<td>26</td>
<td>♀</td>
<td>16 Mild exertional dyspnea</td>
<td>Tall, thin; grade IV/VI, late systolic murmur</td>
</tr>
<tr>
<td>W.K.</td>
<td>23</td>
<td>♂</td>
<td>Birth Slight exertional dyspnea</td>
<td>Tall, thin; grade III/VI, late systolic murmur, initiated by click</td>
</tr>
<tr>
<td>G.L.</td>
<td>35</td>
<td>♂</td>
<td>25 Mild dyspnea on severe exertion</td>
<td>Unremarkable body habitus; grade III/VI, late systolic murmur</td>
</tr>
<tr>
<td>M.S.</td>
<td>31</td>
<td>♀</td>
<td>31 Mild dyspnea</td>
<td>Unremarkable body habitus; grade II/VI, late systolic murmur</td>
</tr>
<tr>
<td>C.M.</td>
<td>57</td>
<td>♂</td>
<td>52 Rapid irregular heart action, easy fatigability, weight loss, effort intolerance, and ankle swelling</td>
<td>Unremarkable body habitus; atrial fibrillation; hyperactive precordium; apex occupied by left ventricle at anterior axillary line; apical systolic thrill; harsh grade IV/VI pansystolic murmur radiating to back; loud third heart sound</td>
</tr>
<tr>
<td>D.D.</td>
<td>53</td>
<td>♂</td>
<td>29 Palpitations and exertional dyspnea</td>
<td>Unremarkable body habitus; grade IV/VI pansystolic murmur</td>
</tr>
<tr>
<td>G.P.</td>
<td>43</td>
<td>♂</td>
<td>28 Exertional dyspnea and easy fatigability; occasional nocturnal dyspnea</td>
<td>Unremarkable body habitus; grade IV/VI pansystolic murmur at apex; grade I/VI mid-diastolic apical murmur</td>
</tr>
</tbody>
</table>

three. The remaining three patients had pansystolic murmurs and third heart sounds. In one, the pansystolic murmur was louder during late systole. The first heart sound was normal or increased in intensity in all of these patients, while the second heart sound was intact, with its two components behaving normally. None of the patients had any evidence of congestive heart failure at cardiac catheterization.

Phonocardiographic Features

Phonocardiograms were recorded on all patients, using either a Sanborn Twin-beam
or multichannel recorder. In 11 patients, recordings were also made following the inhalation of amyl nitrite.

The characteristic appearance of the late systolic murmur and one which was initiated by a click are shown in figure 1. The typical and unique response to amyl nitrite in these patients was a change in the murmur from late systolic to either mid-systolic or pansystolic (figs. 2 and 3). The intensity of the murmur remained unchanged, but on occasion there was slight diminution. Inhalation of amyl nitrite was also used in two of the three patients with pansystolic murmurs. Instead of the expected decrease, there was a slight increase in the intensity of the regurgitant murmur (fig. 4).

**Electrocardiographic Features**

In the majority of patients, the electrocardiogram was normal. In four patients, T waves were negative in leads II, III, and aV_{F} (fig. 5) and in the three patients with severe mitral insufficiency, there was electrocardiographic evidence of left ventricular hypertrophy.

**Roentgenographic Features**

The cardiac silhouette was normal in 11 patients, while the left atrium and ventricle were considered large in the three patients.
The typical late systolic murmur (LSM) becomes a pansystolic murmur following inhalation of amyl nitrite.

In this patient, who already had free mitral regurgitation, the inhalation of amyl nitrite led to a slight increase in the intensity of the murmur. Note its slight ejection contour.
Electrocardiogram showing the common finding of inverted T waves in leads II, III, and aVF.

Figure 5

Figure 6

Left ventricular angiogram, in the left anterior oblique projection, showing the typical billowing leaflet deformity of the mitral valve (MV) without any mitral regurgitation.

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with severe mitral insufficiency. Left ventriculography was performed on all patients. In the two without systolic murmurs, the typical billowing deformity of the mitral valve was present, but the valve was fully competent (fig. 6). In the nine patients with late systolic murmurs, late mitral insufficiency was observed in association with the identical billowing leaflet deformity of the mitral valve (fig. 7). In the three patients with pansystolic murmurs, prolapse of billowing leaflets occurred simultaneously, with passage of contrast media across the ativoventricular plane into the left atrium with the initiation of left ventricular ejection. In the last patient with late mitral insufficiency, a repeat left ventriculogram was made after inhalation of amyl nitrite. This showed the mitral regurgitation to be earlier in onset and greater in magnitude. In the two patients without mitral
insufficiency, supravalvular aortograms revealed large, deep sinuses of Valsalva with a moderate aortic leak in one of them.

**Hemodynamic Studies**

Mild pulmonary hypertension was present in one patient (C. M.); this was associated with the finding in the pulmonary capillary pulse of a v wave measuring 35 mm Hg. Left ventricular end-diastolic pressure was slightly raised in two patients (C. M. and D. D.). The resting cardiac index was low in five patients (C. M., G. P., R. B., A. G., and J. M.). Observations were also made in five patients (G. P., P. H., M. D., G. L. and W. K.) during moderate supine leg exercise using a Collins bicycle ergometer. In the four patients who had late systolic murmurs and late mitral insufficiency (P. H., M. D., G. L., and W. K.) pulmonary artery, pulmonary capillary, and left ventricular end-diastolic pressures remained in the normal range, although there was a moderate rise in all three values. The exercise cardiac index was normal in three of these patients (G. L., W. K., and M. D.) and inadequate for the observed rise in oxygen consumption in one (P. H.). In patient G. P., who had severe mitral insufficiency, moderate supine leg exercise led to mild pulmonary hypertension, a rise in left ventricular end-diastolic pressure to an abnormal value, and a depressed cardiac index when compared to the level of oxygen consumption achieved.

**Observations at Surgery**

The three patients (C. M., D. D., and G. P.) with pansystolic murmurs and severe mitral valve insufficiency were operated upon. At that time, they were severely disabled, with marked effort intolerance and easy fatigability. The surgeons stated that the mitral valve leaflets were extremely large and that they had prolapsed into the left atrium on ventricular contraction. Marked elongation of chorade tendineae was also noted by them.

**Pathological Observations**

Examination of the excised mitral valve leaflets, chordae tendineae, and papillary muscle failed to produce evidence of rheumatic disease or bacterial endocarditis. Instead, extensive myxomatous degeneration of the leaflets and chordae tendineae was found (fig. 8).

**Surgical Follow-up**

To date these three patients have been observed for 58 months, during which time there has been no clinical evidence of mitral insufficiency or prosthetic valve dysfunction.

**Comment**

Until recently, myxomatous valvular changes have been regarded as pathognomonic of Marfan’s syndrome. The three patients who had mitral valve surgery were found to have myxomatous degeneration of the mitral leaflets and chordae tendineae but none of the other features suggestive of Marfan’s syndrome. Similar pathological findings were reported by Read and associates in five patients with mitral insufficiency, in three with aortic insufficiency, and in one patient whose cardiac valves were competent. Although some of the physical features were suggestive of...
Marfan’s syndrome, none of their patients had typical cases. Of the 14 patients described in this paper, only one had typical features of Marfan’s syndrome. Six others who were tall and thin had no arachnodactyly or ocular signs.

Studies by Pomerance\(^7\) of 805 hearts showed that myxomatous valvular changes were not rare and that they occurred in all age groups. The severity of the condition varied from localized areas of degeneration, to gross ectasia, with prolapse of the voluminous cusps into the atrium in systole. However, severity of this degree was not common, and the exact number of specimens showing such changes was not stated by Pomerance. Nevertheless, attention was drawn to the fact that the mural leaflet of the mitral valve often showed the most striking changes, an observation which favors the clinical impression that the mural cusp is involved in prolapse more frequently than the aortic cusp.

The etiology of myxomatous changes in patients without Marfan’s syndrome is unknown. It seems unlikely that aging of leaflets is the responsible factor, since many of the patients studied were young. It has been suggested by Sinclair and associates\(^8\) that various expressions of Marfan’s syndrome may be present in a given patient, so that typical cardiac and vascular abnormalities may dominate in the absence of skeletal or ocular defects. An alternate hypothesis based on studies of valvular striated muscle by Sonnenblick and associates\(^9\) has been put forward by Behar and associates.\(^10\) This is that the observed degenerative changes may be the

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Figure 8

Sections from resected mitral valve. (A) A low-power view showing the large area of myxomatous degeneration. (B) A high-power view showing the characteristic myxomatous material.
result of inability of amuscular mitral leaflets to maintain tension and hence withstand the higher ventricular systolic pressure.

A possible explanation of the late systolic murmur in the patients reported in this paper would be that the chordae, diseased and already longer than normal, are stretched during systole as the left ventricle diminishes in size. Thus, a point would be reached at which the chordae would allow prolapse of a leaflet, so that the varying length of the late systolic murmur would depend on the point at which prolapse occurs during ventricular systole. The importance of changes in size of the left ventricle was illustrated by the response of these patients to the inhalation of amyl nitrite. In seven of the nine patients with late systolic murmurs, the murmur became pansystolic, a finding which agrees with that of Hancock and Cohn. Similar responses to inhalation of amyl nitrite were described by Vogelpoel and associates and by Barlow and associates in patients with late systolic murmurs. Amyl nitrite, by reducing the size of the left ventricle, causes the elongated chordae to become too long relative to the long axis of the chamber. This implies that the critical pathogenetic factor is the degree of elongation of the chordae tendineae. Whether this lesion of the mitral valve is progressive is one of the prime objects of follow-up studies of these patients.

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References

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