The Structure of the Aortic Valve in Clinically Isolated Aortic Stenosis
An Autopsy Study of 162 Patients Over 15 Years of Age
By William C. Roberts, M.D.

SUMMARY
The structure of the aortic valve at autopsy is described in 162 patients over 15 years of age with clinically isolated, severe valvular aortic stenosis with or without aortic regurgitation. The valves were congenitally unicuspid, unicommissural in 17 patients, congenitally bicuspid in 67, tricuspid in 71, and in seven the structure was uncertain. Thus, in at least 84 (52%) of the patients the valve was congenitally malformed at birth. It is proposed that minor aortic valvular cuspal inequality, also present from birth, may be an underlying malformation in some of the patients with tricuspid stenotic aortic valves. Degeneration or wear-and-tear from aging almost certainly explains aortic stenosis in most of the elderly patients. Although no patient had clinical evidence of mitral valvular dysfunction, the mitral leaflets were diffusely thickened by fibrous tissue in 26 of the 162 patients. Rheumatic disease is believed to be the cause of the valve involvement in 22 of them (the other four had congenitally bicuspid aortic valves). Rheumatic disease did not appear to be the cause of the aortic stenosis in the other 136 patients with anatomically normal mitral valves.

Additional Indexing Words:
Bicuspid aortic valve Cardiac calcification Congenital heart disease
Mitral valvular dysfunction Rheumatic heart disease Unicuspid aortic valve

RECENTLY, the aortic valve has been shown to be congenitally bicuspid in a high percentage of patients with valvular aortic stenosis, and other factors have indicated that anatomically isolated aortic valvular disease is usually not rheumatic in origin. In the present postmortem study the hearts of 162 patients who presented clinically with isolated aortic stenosis with or without aortic regurgitation were reviewed. The prime purpose was to determine how often the aortic valve was congenitally malformed and how often the functionally normal mitral valve was anatomically abnormal.

Patients Studied
Observations in the 162 patients are summarized in table 1. Clinically, each was in functional class III or IV (New York Heart Association classification). Patients less than age 16 years were excluded. The average age was 52 years; 34 patients were older than 60 years of age and 16 were older than 70 years of age. Aortic valve operation (valvuloplasty or partial or total replacement) was performed in 106 patients; the average age of death in them was 49 years. The average age at death of the 56 patients on whom no cardiac operation was performed was 57 years, but 16 of the 20 who were older than 65 years of age were included in this group. The three patients without grossly visible calcific deposits in the aortic valve were aged 16, 24, and 33 years, and the peak systolic pressure gradients between the left ventricle and a
Table 1

Data in Patients with Clinically Isolated Valvular Aortic Stenosis

<table>
<thead>
<tr>
<th>Valve structure</th>
<th>No. of patients</th>
<th>Age range (av)</th>
<th>No. of patients older than 65 yr</th>
<th>Sex</th>
<th>History of ARF or chorea</th>
<th>LV-SA PSG (mm Hg)</th>
<th>Aortic valvular calcium (g)</th>
<th>Heart wt. (g) Range (av)</th>
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<tr>
<td>Unicommissural</td>
<td>17</td>
<td>16-62</td>
<td>0</td>
<td>13</td>
<td>4</td>
<td>10-158</td>
<td>17</td>
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<td></td>
<td></td>
<td></td>
<td>(78)*</td>
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<td>(616)</td>
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<td>Bicuspid</td>
<td>67</td>
<td>16-79</td>
<td>2</td>
<td>48</td>
<td>19</td>
<td>12-165</td>
<td>64</td>
<td>295-1000</td>
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<td></td>
<td></td>
<td></td>
<td>(93)†</td>
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<tr>
<td>Tricuspid</td>
<td>71</td>
<td>21-90</td>
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<td>53</td>
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<td>(84)†</td>
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<td>(643)</td>
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<td>MV normal</td>
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<td>28-90</td>
<td>16</td>
<td>34</td>
<td>15</td>
<td>20-160</td>
<td>49</td>
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<td>(595)</td>
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<td>MV leaflets thick; CT normal</td>
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<td>39-76</td>
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<td>25-120</td>
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<td>MV leaflets and CT thick</td>
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<td>5</td>
<td>1</td>
<td>20-90</td>
<td>6</td>
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<td>(61)</td>
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<td>(731)</td>
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<td>0</td>
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<td>0</td>
<td>52-105</td>
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<td>(81)§</td>
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<td>(600)</td>
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<tr>
<td>Total</td>
<td>162</td>
<td>16-90</td>
<td>20</td>
<td>122</td>
<td>41</td>
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<td></td>
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<td>(75%)</td>
<td>(25%)</td>
<td>(87)</td>
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<td>(619)</td>
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</table>

*10 patients; PSG < 50 mm Hg in two.
†52 patients; PSG < 50 mm Hg in six.
‡49 patients; PSG < 50 mm Hg in seven.
§5 patients; PSG < 50 mm Hg in none.

Abbreviations: ARF = acute rheumatic fever; CT = chordae tendineae; LV = left ventricle; MV = mitral valve; PSG = peak systolic gradient; SA = systemic artery.
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Figure 1

Stenotic unicommissural unicuspid aortic valves from above in two patients. (a) The valve in this 48-year-old man (A68-101) is severely stenotic and heavily calcified. (b) Same patient as a. The heart weighed 750 g. (c) The valve in this 62-year-old man (A69-276) also is severely stenotic, but the heart weighed 400 g. In contrast to the valve shown in a, two false commissures are present in addition to the one true commissure.

systemic artery in them were 80, 150, and 160 mm Hg, respectively.

The 162 patients were divided into four groups depending on the structure of the aortic valve. Representative valves are illustrated in figures 1 to 3. The excised valves in all patients who had undergone valve replacement also were re-examined (most had been removed intact). The prosthetic aortic valve in each, however, was removed so that the number of lateral attachments (commissures) of the cusps to the aorta could be determined.

Figure 2

Stenotic congenitally bicuspid aortic valves from above in two patients. (a) The valve in this 61-year-old man (A64-155) contains a raphe in the anterior cusp. The peak systolic left ventricular-to-systemic arterial pressure gradient across this valve 2 years before death was 45 mm Hg. The heart weighed 700 g. (b) The valve in this 56-year-old woman (A70-6) was operatively debrided of calcific deposits a day before death. The peak systolic pressure gradient across the valve preoperatively was 47 mm Hg. The cusps are located on the right and the left, respectively. The heart weighed only 295 g.
In 17 patients the aortic valve was unicommissural and unicusp. In a few of the 17, two raphes (false commissures) were visible, but in most no raphe was present.

In 67 patients the aortic valve was congenitally bicusp. Two basic types of bicusp valves were seen: (1) In 54% of subjects the two cusps were located right and left, the commissures anteriorly and posteriorly, and a coronary artery arose from behind each cusp. (2) In 46% of the patients the two cusps were located anteriorly and posteriorly, the commissures, on the right and left, and both coronary arteries arose in front of the anterior cusp. Raphes were clearly visible in half the valves. When the cusps were located on the right and the left, the false commissures were always in the right cusp; when the cusps were located anteriorly and posteriorly, the raphe was always in the anterior cusp. In several patients with congenitally bicusp aortic valves one true commissure was fused, producing in essence an acquired unicommissural aortic valve. The valves were divided, however, according to their original structure.

The 71 patients with tricuspid aortic valves were subdivided according to whether the mitral leaflets and chordae tendineae were normal or thickened by fibrous tissue. In 49 patients (69%), the mitral leaflets and chordae were entirely normal. Sixteen (33%) of these 49 patients were over 65 years of age whereas only four (4%) of the remaining 113 with aortic stenosis were over 65 years of age. In at least three of the 49 patients the aortic valve cusps were unequal in size and one of them also had a congenitally bicusp pulmonic valve. In 16 of the 71 patients with tricuspid aortic valves the mitral valve leaflets were diffusely although mildly thickened and the mitral chordae tendineae were normal. Nine of these 16 patients had positive histories of acute rheumatic fever or chorea whereas only one of the 49 with tricuspid aortic valves and normal mitral valves had positive histories. In six of the 71 patients with tricuspid aortic valves the mitral chordae tendineae as well as the mitral leaflets were diffusely but mildly thickened, and four of them had positive histories of acute rheumatic fever or chorea. (The mitral valve was normal in each of the 17 patients with unicommissural aortic valves and in 62 of the 66 with congenitally bicusp valves. In the other four, the leaflets were

Figure 3

Stenotic three-cuspid aortic valves in two patients. (a) Each of the three commissures are fused in this stenotic and incompetent valve of a 49-year-old man (A58-19). The peak systolic pressure gradient across the valve was 74 mm Hg and the heart weighed 600 g. (b) This valve is from an 80-year-old woman who had clinical features of severe aortic stenosis. One commissure is fused but only minimally. The cusps are made relatively immobile by calcific deposits only. The heart weighed 400 g.
diffusely but mildly thickened, and the chordae were normal. In each of the seven patients in whom aortic valve structure was uncertain the mitral valve was normal.)

In seven of the 162 patients the underlying structure of the aortic valve was uncertain. Each of these patients had heavily calcified valves, and each had been excised and replaced by a prosthesis. The valves in them were not excised intact, and the number of commissures on the wall of the aortic root was unclear after removing the prosthesis.

At least four histologic sections of myocardium were examined in all 162 patients, and none had Aschoff bodies.

Discussion

The data show that among adults with clinically isolated valvular aortic stenosis with or without aortic regurgitation the aortic valve is congenitally bicuspid in 43%, tricuspid in 46%, and congenitally unicommissural, unicuspid in 11%. Thus, 54% of the patients in whom the aortic valve structure was discernible had congenitally bicuspid or unicuspid aortic valves. The mitral valves were normal in 136 (84%) and thickened in 26 (16%). Of the 136 patients with normal mitral valves, seven (5%) had positive histories of acute rheumatic fever or chorea whereas 13 (50%) of the 26 with thickened mitral valves (including four with congenitally bicuspid aortic valves) had positive histories.

Although the structure of the aortic valves in 96% of the described patients was clear, the cause of the valvular obstruction in most of them is less clear. Without question a congenital malformation was the underlying valve disturbance in the 17 patients with unicommissural valves, in the 67 with bicuspid valves, and probably also in the seven whose valve structure was uncertain. Although the valvular malformation was congenital, the valvular obstruction may or may not have been present from the time of birth. Edwards has stated that the congenitally unicommissural aortic valve is inherently stenotic and that the unicuspid valve is the only type of valve stenotic at the time of birth. Of the 17 patients with congenitally unicommissural aortic valves described herein, each was stenotic, none was purely incompetent, and only one patient had had a history of infective endocarditis. Edwards has contended that the congenitally bicuspid valve, in contrast to the unicuspid one, is not stenotic at birth but becomes stenotic only as it becomes fibrotic and calcified. In contrast to the congenitally unicommissural aortic valve, however, the congenitally bicuspid aortic valve may be

Figure 4

Shown here are opened, functionally normal aortic valves in five patients with unequal-sized cusps. Note the differing distances between the commissures in the patients. (a) Age 4 years. (b) Age 21 years. (c) Age 7 years. (d) Age 36 years. (e) Age 60 years. All five patients died of noncardiac conditions (leukemia [a and c], lymphoma [d and e], and cystic fibrosis of pancreas [b]).

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Diagrammatic portrayal of equal and unequal-sized aortic valve cusps. (Top row) The cusps of the aortic valve are equal in size and the circumferential distances between the commissures are equal. The straight-line distances between the commissures (as indicated by the dashed lines in the center circle) also are equal. On the right the aortic valve is opened. (Middle row) Here the cusps are of unequal size, and they are made unequal by differing cephalocaudal lengths of the individual cusps. The distances between the commissures circumferentially around the aorta and the straight-line distances within the lumen of the aorta are similar to the normal shown in the top panel. (Lower row) Here not only are the cephalocaudal lengths of the individual cusps different, but the circumferential distances around the aorta and the straight-line distances within the lumen of the aorta between the commissures (lateral attachments) are different.

purely incompetent, may be more often the site of infective endocarditis, and may function normally for an entire lifetime without developing any complication (stenosis, incompetence, or infection). The cause of the aortic stenosis in many of the 71 patients with tricuspid aortic valves is speculative. It is reasonable to believe that the etiology is rheumatic in most or all of the 22 patients with associated anatomic disease of the mitral valve. In addition to the anatomic mitral valvular involvement, the incidence of positive histories of acute rheumatic fever in them was high (60%). The cause of the aortic stenosis in the 49 patients with tricuspid aortic valves and normal mitral valves is almost certainly not rheumatic. Only one of the 49 patients had a positive history of acute rheumatic fever or chorea. Healed infective endocarditis likewise seems unlikely from anatomic study of the valves and from the lack of a positive history of infective endocarditis in any patient. No patient had a recorded history of, or anatomic evidence of, brucellosis. Could the aortic valve be tricuspid and still congenitally malformed? At least three of the 49 patients clearly had aortic valve cusps of unequal size. The pulmonic valvular cusps
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are of slightly unequal size in most normal subjects.6 Cuspal inequality in the low pressure right side of the heart is obviously of no consequence. Similar inequality of cuspal size in the high pressure left side of the heart, however, may be far more important. Unequal-sized aortic valve cusps are occasionally observed at autopsy in individuals dying of noncardiac conditions (fig. 4). When the cusps become severely fibrotic, nodular, calcified, or focally contracted, however, cuspal inequality probably is difficult to appreciate. This thesis of minor aortic cuspal inequality as an underlying congenital malformation in adults with valvular aortic stenosis is expanded in figure 5.

Fibrosis and calcification of the three aortic valve cusps as a consequence of aging (wear-and-tear) is almost certainly the explanation of the aortic stenosis in a significant percentage of the subjects with three-cuspid aortic valves and intrinsically normal mitral valves. Sixteen of the 49 patients with aortic stenosis, three-cuspid aortic valves, and normal (except for expected age changes) mitral valves were over 65 years of age. In addition to heavy calcific deposits in the aortic valve in these 16 patients, 14 also had calcific deposits in the mitral annulus and subvalvular angle beneath the posterior mitral leaflet, and all 16 had calcific deposits in the walls of one or more of the three major extramural coronary arteries. Commisural fusion in the older patients was unusual. None had positive histories of acute rheumatic fever or chorea. It seems most reasonable to believe that the aortic valvular calcification and stenosis in these 16 patients is on the basis of aging or degeneration.

Acknowledgment
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