CLINICOPATHOLOGIC CORRELATIONS

Bacterial Endocarditis in Subjects 60 Years of Age and Older

By Rudy Thell, M.D., Franklin H. Martin, M.D., and Jesse E. Edwards, M.D.

SUMMARY

Forty-two cases of bacterial endocarditis with pathologic confirmation are reviewed. Infection was restricted to one or both left-sided valves in 31 cases, right-sided valves in five cases, and valves in both sides of the heart in six cases. In those specimens available for review, underlying valvular disease was identifiable in 24 of 38 cases (63%). The common underlying diseases, in order of decreasing frequency, were calcified or otherwise deformed aortic valves (11 cases) and rheumatic fibrosis of the mitral valve (eight cases). The floppy mitral valve was the underlying condition in two cases and amyloid infiltration of the tricuspid valve in one.

Among the 34 cases from which a specific organism was identified, the dominant organisms were Staphylococcus (14 cases) and various types of Streptococci (ten cases). Fungi were the causative organisms in two cases.

The clinical suspicion for the presence of bacterial endocarditis was low (40% of 40 cases with adequate data). In those cases with adequate data, murmurs were present in 68% and fever in 93%. Of those patients with fever, clinical diagnosis was made or suspected in only 38%. When a murmur was present, the clinical diagnosis was made or suspected in 54% of the cases, while when a murmur was absent the disease was suspected in only 9% of the cases.

The clinical diagnosis of bacterial endocarditis in older subjects depends upon 1) knowledge that the disease may occur in such subjects and 2) recognition that, although fever is commonly present, murmurs may be absent.

Additional Indexing Words:
Calcific aortic stenosis  Bicuspid aortic valve  Billowing mitral valve
Cardiac amyloidosis  Fungal endocarditis

ALTHOUGH THE MAJORITY of instances of bacterial endocarditis occurs between the third and seventh decades of life, a significant number of cases occurs in individuals over 60 years of age. In 1955, Anderson and Staffurth found that patients in the fourth decade of life represented the most common age group (22.4%) among subjects with bacterial endocarditis. In that study, 11.8% of cases occurred in subjects between 60 and 69 years of age and 6.6% in those between 70 and 79 years of age. In reviews by Lerner and Weinstein and Weinstein and Rubin, it is shown that bacterial endocarditis has become more common in older age groups in recent years than in the past. In the observations of Lerner and Weinstein, 30% of patients with bacterial endocarditis were 60 years of age or older.

It is often reported that the clinical diagnosis of bacterial endocarditis is less commonly made in older subjects than in younger subjects. Anderson and Staffurth indicated that the reasons for this discrepancy include the facts that 1) it is not generally realized that the disease may occur in this age group, 2) the disease may be less severe in the aged, and 3) several of the usual criteria are not necessarily found in the aged. Bayles and Lewis, in 1940, reporting on bacterial endocarditis in subjects 40 years of age or older, indicated that the manifestations of this disease in older subjects are the same as in younger subjects, but less accentuated.
We reviewed 42 cases of infective endocarditis* in subjects 60 years of age or older from which we had an opportunity to review the pathologic features. In one case the infection had healed but was active in the remaining cases. Over a 14-year period, beginning June 1, 1960, the specimens were derived from a number of sources, principally the Miller Division of United Hospitals, the University of Minnesota Hospitals, and the Hennepin County General Hospital. Specimens were available for restudy in all but four of the cases.

The primary purpose of this review was to emphasize the occurrence of this disease in the age group concerned. The review also considers the sites of primary valvular infection, underlying valvular diseases and organisms involved, as well as a summary of certain clinical features. In the latter area, we are concerned with whether fever and murmurs were present and whether there had been clinical suspicion of the disease that was identified pathologically.

In 41 subjects, the disease was confirmed at autopsy and in one from a surgically resected valve. The ratio of male to female subjects was about 2:1 (29 males, 13 females). The ages of the patients were as follows: 24 subjects were in the seventh decade, 16 in the eighth, two in the ninth, the oldest patient being 89 years of age.

Valves Involved and Primary Sites of Infection

When more than one valve is involved it is not always possible to determine with certainty which valve represents the primary site of infection. Yet this

*In two cases, the disease was caused by fungal organisms but for convenience of expression the term bacterial endocarditis will be applied to these cases, as well as to those caused by bacteria.

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mitral valve alone in 11, and both the mitral and aortic valves in six. In five of the latter, we considered that the infection had involved the aortic valve primarily and the mitral valve secondarily. In the sixth case the aortic endocarditis was considered to be secondary to primary infection of the mitral valve. Using these interpretations, the aortic valve was the primary site of infection in 19 and the mitral in 12 of the 31 cases with infection restricted to the left-sided valves.

Infection restricted either to one or both right-sided valves was observed in five instances. In each instance the tricuspid valve was infected and considered to be the primary site of infection. In one of these the pulmonary valve was also infected. We did not observe any cases with infection restricted to the pulmonary valve.

Infection of one or more valves in each side of the heart was observed in each of the remaining six cases. These cases deserve special consideration.

In the first case, the patient had beta streptococcal septicemia and was treated with penicillin and tetracycline. After ten days of treatment, blood cultures yielded Candida albicans for which the patient was then treated with amphotericin B. After death, pathologic signs of endocarditis were found involving the mitral and tricuspid valves with coci identified histologically. Signs of preceding rheumatic fibrosis were identified in the mitral valve and this valve was considered to be the primary site of infection.

In the second case, a congenital bicuspid aortic valve was calcified and stenotic. Infection of this valve with Listeria monocytogenes complicated renal dialysis for chronic renal failure. Extension of infection from the primarily infected aortic valve had occurred through the base of the ventricular septum to involve the tricuspid valve secondarily.
Table 1

<table>
<thead>
<tr>
<th>Underlying valvular disease</th>
<th>Left-sided primary site of infection</th>
<th>Right-sided primary site of infection</th>
<th>Bilateral valves</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aortic</td>
<td>Mitral</td>
<td>Tricuspid</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Calcific aortic stenosis</td>
<td>5*</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Noncalcified bicuspid-unicuspid aortic valve</td>
<td>5†</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Rheumatic fibrosis</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>2†</td>
</tr>
<tr>
<td>Floppy valve</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Amyloid</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Aortic valve prosthesis</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Heart not available</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>12</td>
<td>5</td>
<td>42</td>
</tr>
</tbody>
</table>

*Includes two congenital bicuspid aortic valves, two acquired bicuspid aortic valves, and one senile calcific aortic stenosis.
†Includes three acquired bicuspid aortic valves, one congenital bicuspid aortic valve, and one congenital unicuspid aortic valve.
‡Calcified congenital bicuspid aortic valve primary site of infection.
§Mitral valve involved in underlying disease and in primary infection.
¶Primary site of infection on tricuspid valve in one case. In two cases primary site of infection not determined.

Figure 5

Bacterial endocarditis of the mitral valve in a 75-year-old woman. Infective organism was Staphylococcus aureus. a) Left atrium and left ventricle. The mitral leaflets show mild thickening, as do some of the chordae, a picture consistent with mild residual effects of rheumatic endocarditis. In addition to vegetations on the base of the posterior mitral leaflet, there is a defect in the posterior wall of the left atrium representing regurgitant infection at that site. b) Photomicrograph of a section through posterior mitral leaflet and related walls of left atrium (L.A.) and ventricle (L.V.). Inflammatory process at base of leaflet and left atrium. (Elastic tissue stain; × 2.3)
In the third case there was underlying rheumatic disease of the mitral valve. Infection with a gamma Streptococcus involved this valve as well as the aortic and tricuspid valves. The mitral valve was considered to be the primary site of infection.

In the fourth case, cultures had not been done but gram positive cocci were obtained at autopsy from vegetations upon the tricuspid, pulmonary, and mitral valves. No underlying disease was identified. In view of the fact that numerous septic emboli and abscesses were found in the lungs, a right-sided valve (probably the tricuspid) was considered the primary site of infection, the other two valves involved being considered secondarily infected.

In each of the remaining two cases with involvement of valves in both sides of the heart, there was no identifiable background disease. Organisms were identified by culture in both. Alpha Streptococcus was recovered during life from the blood of one patient. In the other, antemortem blood cultures had given negative results but postmortem blood cultures yielded both alpha Streptococcus and Aerobacter aerogenes. In these two cases, no firm determination seemed possible as to the site of primary infection.

Underlying Valvular Disease

When a valve becomes infected, minor underlying disease of the valve may be obscured by the inflammatory process, including its reactive phase. Nevertheless, it is possible in most instances to determine, with a reasonable degree of certainty, whether some abnormality of the valve had been present prior to the onset of infection (table 1).

The concept that bacterial endocarditis almost always develops on sites of previous disease is giving way to recent observations that this disease may occur on previously normal valves. In the series by Lerner and Weinstein, 2 39% did not show an underlying valvular disease. According to Buchbinder and Roberts, 5 in 1972, 53% of cases did not show preexisting disease. Wallach et al., 6 in 1955, observed a lower average age in subjects without underlying rheumatic endocarditis than in those without underlying disease.

In our series, no underlying disease was identifiable in 14 (37%) of 38 cases in which the specimen was available for reexamination (fig. 1).

In the aortic valve, which was the most common site of primary infection, the two most common types of underlying disease were calcific aortic stenosis, six cases, (fig. 2) and deformed, noncalcified aortic valve, five cases. In the five cases with noncalcified, deformed aortic valves, the underlying conditions took the following forms. In one case there was a congenital unicuspid aortic valve (69-year-old man) (fig. 3) and in four cases the valves were bicuspid (fig. 4). Of the latter, the bicuspid aortic valve was considered to be acquired in three cases and congenital in one.

In various reports arteriosclerotic heart disease is listed as a cause of underlying valvular disease. 7 It is probable that the aforementioned term is used for some type of aortic valvular calcification, possibly that which commonly is seen in the aortic valve in subjects over 60 years of age.

Rheumatic fibrosis of valvular tissue without calcification was considered to be the background disease in eight cases (seven mitral, one aortic) (fig. 5).

The floppy or billowing mitral valve was observed in two cases as an underlying disease (fig. 6). It is of interest that Wunsch et al. 8 described a case of mitral valvular endocarditis caused by an alpha Streptococcus in an 18-year-old male patient with Marfan’s syndrome. These authors stated that five other cases of
Organisms

In 40 of the 42 cases, organisms were identified by culture, histologic examination or both (table 2). Of the two cases in which organisms were not identified, one involved perforation of the aortic valve, the process appearing as an example of healed bacterial endocarditis (fig. 8). The other was a case of calcific aortic stenosis. Although an active inflammatory process involved this valve, no organisms were identified histologically. In six other cases unspecified types of gram positive cocci were identified, one from an antemortem blood culture. In the remaining five

bacterial endocarditis complicating Marfan’s syndrome had been reported earlier.

In one instance, tricuspid endocarditis caused by Candida occurred in a case with cardiac amyloidosis in which the valve was heavily involved with the abnormal infiltrate (fig. 7).

In two cases infection complicated the presence of prosthetic valves, each aortic. One infection was observed in a patient dying seven days postoperatively (Escherichia coli and Klebsiella, postmortem growth) and the other in a subject dying 14 days after operation (enterococcus).

Amyloidosis and Candida endocarditis of the tricuspid valve in a 75-year-old man. a) Left atrium (L.A.) and left ventricle (L.V.). The atrial endocardium is speckled, a picture characteristic of cardiac amyloidosis. b) Right atrium (R.A.) and right ventricle (R.V.). The right atrial endocardium as well as the tricuspid leaflets are speckled with foci of amyloid. Large vegetations of an infective endocarditis are present on the tricuspid valve. Between the arrows is a pale zone representing amyloid infiltration of the tricuspid valve, on the surface of which are vegetations of infective endocarditis. (Elastic tissue stain; × 33.3) d) Photomicrograph of a vegetation of the tricuspid valve showing blastospores of Candida. (PAS stain; × 293.3)
cases such organisms were identified upon histologic examination of valvular tissue and vegetations. This left 34 cases from which organisms were specifically identified, either from antemortem blood cultures (27 cases) or postmortem culture of blood and/or vegetations (seven cases).

Of the seven cases from which organisms were obtained only during the postmortem examination, antemortem blood cultures had not been done in five and were negative in the other two.

In 32 of the 34 cases from which organisms were recovered, the organisms were bacteria, while in two they were fungal in type, one being Torulopsis and the other an unidentified type of Candida.

The two most common types of bacteria in order of decreasing frequency were staphylococci (14 cases) and streptococci (ten cases). The dominant type of streptococci were as follows: alpha, six cases; beta, three cases; and gamma, one case.

The high incidence of staphylococcal infection, relative to those caused by streptococci, probably reflects changing patterns as to causative organisms observed in all age groups.9

In four cases, less common types of bacteria causing bacterial endocarditis were recovered. Escherichia coli, Diplococcus pneumoniae, Pseudomonas and Listeria monocytogenes were each found in one case. The recovery of fungi as causes of primary infection in two of 34 cases may reflect an increasing incidence of fungal endocarditis as a result of common use of antibiotics as suggested by Zimmerman10 and by Alderson and Bernhardt.11

From each of four cases, two organisms were recovered. In one case, such results were obtained in antemortem blood cultures, the organisms being

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Table 2
Organisms Identified as Bacterial Endocarditis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Left-sided valves only</th>
<th>Right-sided valves only</th>
<th>Bilateral valves</th>
<th>Total</th>
</tr>
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<td></td>
<td>Primary site of infection</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aortic</td>
<td>Mitral</td>
<td>Tricuspid</td>
<td>Mitral</td>
</tr>
<tr>
<td>Streptococcus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Viridans</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Enterococci</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Undetermined</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Beta</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gamma</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total streptococcus</td>
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<td>3</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aureus</td>
<td>4</td>
<td>6</td>
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<tr>
<td>Epidermidis</td>
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<td>0</td>
<td>0</td>
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<tr>
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<td>0</td>
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<td>Total staphylococcus</td>
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<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Unidentified gram positive cocci</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mixed flora</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other uncommon bacterial organisms</td>
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<td>1</td>
</tr>
<tr>
<td>Fungal</td>
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<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Organism not identified</td>
<td>2</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>Totals</td>
<td>19</td>
<td>12</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

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Figure 8
Healed bacterial endocarditis of the aortic valve. The right aortic cusp shows a perforation which is capped by a vegetation. The opposing left cusp shows a smaller perforation as well. The patient was a 74-year-old man. Causative organism is unknown.
alpha Streptococcus and gram negative bacilli. In the other three cases with mixed flora, the organisms were obtained at autopsy. In two of these cases antemortem blood cultures had given negative results. The postmortem-obtained organisms per case were the following: enterococcus and Escherichia coli, Klebsiella and Escherichia coli, and enterococcus and Aerobacter aerogenes. It is likely that the second named organism of each of the combinations was a contaminant.

**Clinical Features**

The available clinical data of 40 patients were reviewed with regard to the physician’s suspicion of the presence of bacterial endocarditis, the presence of fever and of murmurs.

It is of interest that clinical diagnosis was made or suspected in only 16 cases, while the diagnosis was not suspected in 24 (60%). There seemed to be no inordinate difference for the suspicion, or lack of it, with regard to the side of the heart involved. The relatively high incidence of lack of suspicion of bacterial endocarditis in older individuals observed in this study is similar to the reports of others.7

Records of body temperature of 100° (oral) or greater were identified as fever in this study. Among 31 cases in which pertinent data were available, there were only two that did not show fever according to our definition. Yet among the 29 with fever and data as to the clinical diagnosis, the diagnosis of bacterial endocarditis was made or suspected in only 11 cases (38%).

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*Figure 9*

Bacterial endocarditis of tricuspid and pulmonary valves caused by an unidentified gram positive coccus. The patient was a 71-year-old man. The mitral cvalve was also affected. a) Tricuspid valve. Vegetations are present on the septal and anterior leaflets (latter has been sectioned). b) Pulmonary valve. One cusp which is partially prolapsed shows vegetations attached to its free aspect. c) Vegetation of pulmonary valve shows numerous colonies of cocci. (H & E; × 33.3) d) Large pulmonary muscular artery. Septic embolus and secondary acute arteritis. (H & E; × 33.3)
Data on cardiac murmurs were available in 35 cases. Murmurs of some type were present in 24 (68%) and absent in 11. In 13 cases (54%) with a murmur, the diagnosis was made or suspected clinically, while among the 11 without a murmur the clinical diagnosis was made or suspected in only one (9%). It is to be emphasized that among cases of right-sided endocarditis, murmurs are commonly absent while fever and signs of pulmonary infection dominate the clinical picture.\(^\text{12}\) (fig. 9).

References
Bacterial endocarditis in subjects 60 years of age and older.
R Thell, F H Martin and J E Edwards

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