Bacterial Endocarditis Following Aortic Valve Replacement

Clinical and Pathologic Correlations

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In recent years numerous devices for prosthetic replacement of the diseased mitral or aortic valve have been developed. With their application, both stenotic and regurgitant malformations may be effectively corrected, and although most patients derive gratifying clinical and hemodynamic benefit, many complications may alter the postoperative course of a patient with a prosthetic cardiac valve. Among those most feared is the development of infectious endocarditis. In reported experiences, such infections, whether dating from the time of operation or occurring in the late postoperative period, have almost always proved to be fatal. 1-4 At the National Heart Institute, prosthetic mitral or aortic valves, or both, have been utilized in more than 200 patients, and none has developed endocarditis during the early postoperative period. Three patients who had had aortic valve replacement, however, developed bacterial endocarditis a number of months after operation. In each of them the infection resulted in detachment of the prosthetic valve and massive, fatal aortic regurgitation. The clinical and pathologic findings in these patients are described, and the advisability of secondary operative treatment in patients with infected prosthetic valves is discussed.

Clinical and Pathologic Findings

H. L. (03-44-81), a 57-year-old man, had calcific aortic stenosis and regurgitation, and in November 1962, the aortic valve was replaced with a flexible Teflon prosthesis. His immediate postoperative course was uneventful, he evidenced marked clinical improvement, and 6 months after operation cardiac catheterization revealed only a trivial pressure gradient across the prosthetic valve. In December 1963, all of his teeth were removed; at this time he was given 600,000 units of procaine penicillin intramuscularly twice daily for 3 days before and for 4 days after the procedure. In May 1964, he was fitted with dentures. He remained well until June 1964, when he experienced the onset of exertional dyspnea, fever, and chills. At another hospital, beta hemolytic Streptococcus was grown from several blood cultures. He was treated with intravenous penicillin (20 million units daily) for 4 weeks, but remained febrile, and on July 23, 1964, he was readmitted to the National Heart Institute. He was in acute left- and right-sided heart failure, had loud precordial murmurs characteristic of aortic stenosis and aortic regurgitation, splinter hemorrhages, splenomegaly, and anemia. The blood pressure was 150/50 mm. Hg. Chest roentgenograms revealed that the heart was distinctly larger than it had been previously. Numerous blood cultures were sterile. Despite daily administrations of penicillin (40 million units intravenously), kanamycin (1 Gm. intramuscularly), streptomycin (2 Gm. intramuscularly), and chloramphenicol (4 Gm. intravenously), his condition failed to improve and he died on August 14, 1964.

At autopsy (A64-148), the right and noncoronary leaflets of the Teflon aortic valve were found to be partially detached from the annulus (fig. 1), and two of the suspended commissures of the valve had disrupted. Cultures of the necrotic aortic annulus grew a variety of organisms (Candida albicans, Escherichia coli, and Enterobacter and Bacillus species), but no bacteria or fungi were seen in the histologic sections of this area.

F. H. (03-29-09), a 55-year-old man, who had calcific aortic stenosis and regurgitation, had a partial aortic valve replacement in December 1960. Postoperatively, he did well and was asymptomatic until July 1962, when exertional dyspnea and angina pectoris recurred. These symptoms progressed and, on examination and

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at cardiac catheterization, he was found to have severe recurrent aortic regurgitation. In February 1963, he was operated upon again and the prosthetic leaflet was found fragmented; the entire valve was replaced with a tricuspid Teflon prosthesis. Postoperatively, the patient again improved, but, in May 1963, he apparently had an acute myocardial infarction and 2 weeks later developed fever and chills. On readmission there was again evidence of aortic regurgitation; dermal petechiae, splenomegaly, and anemia were present. Chest roentgenograms showed the heart to be larger than it had been previously. Non-hemolytic *Staphylococcus albus*, coagulase negative, was grown from each of six blood cultures. In vitro, the organism was sensitive to penicillin and he was treated daily for 6 weeks with 30 million units intravenously. All blood cultures following the initiation of penicillin therapy were sterile, and the clinical manifestations of active infection disappeared. In July 1964, he was operated upon for the third time. The Teflon prosthesis was largely detached from the aortic annulus, which was partially necrotic. The Teflon valve was removed and replaced with a Starr-Edwards ball valve. Cultures of the aortic annulus

*Figure 1*

Photograph of the Muller-Teflon aortic valve in patient H. L. (left) and photomicrograph of the aortic root (right). Left. The vertical attachment (not seen) of the right (R.) and non-coronary (N) Teflon cusps is completely separated from the aortic wall, and these cusps are largely detached from the aortic annulus (between the arrows). In addition, the suspended commissure between the right and left (L.) cusps is partially detached. Right. Section includes the anterior mitral leaflet (M.V.) and walls of the ascending aorta and left atrium (L.A). The surface of the aorta contains fibrin material but no organisms. A small abscess is located between the aortic valve “annulus” and the mitral valve ring. L.V., left ventricle.
obtained at the time of operation, however, grew *Staph. albus*. Penicillin (20 million units intravenously daily) was given for 3 weeks after the operation. Three weeks after it was discontinued, and while the patient was still in the hospital, he became febrile once more and *Staph. albus* was again cultured from the peripheral blood. Treatment was instituted with methicillin, 20 Gm. intravenously daily, but there was little apparent response to the drug, and after 1 week he suddenly developed acute pulmonary edema, signs of massive aortic regurgitation, and died.

At autopsy (A63-176), the fixation ring of the Starr-Edwards prosthetic valve was found detached around more than half of its circumference (fig. 2). The cage of the prosthetic valve lay within an infected aneurysm of the aorta (figs. 2 and 3). There were large foci of necrosis and numerous abscesses in the periaortic tissues and, although cultures of this area grew multiple organisms (*Torulopsis glabrata*, *Pseudomonas aeruginosa*, *E. coli*, hemolytic *Staphylococcus aureus*), none was visible in histologic sections.

W. L. (04-00-86), a 51-year-old man, had a flexible Teflon prosthetic valve inserted for the treatment of calcific aortic stenosis in January 1962. Initially, he experienced good symptomatic improvement, but 1 year after operation the signs and symptoms of left-sided heart failure reappeared, and precordial murmurs typical of aortic stenosis and regurgitation again became audible.

The patient’s symptoms progressed, and in October 1963 a second operation was performed. There was no evidence of infection, but the Teflon valve was perforated and calcified. It was replaced with a Starr-Edwards valve and the patient made an uneventful recovery. Ten months after operation the patient returned for postoperative study. He was asymptomatic, and there was no clinical or hemodynamic evidence of aortic regurgitation. In September 1964, the patient had several carious teeth extracted, and his physician gave him intramuscular injections of 600,000 units of penicillin on the day before, the day of, and the day after, the procedure. Two days later, however, he developed chills, fever, weakness, and malaise, and during the next 5 weeks lost 6 Kg. in weight and became anemic. On readmission in October 1964 he was acutely ill, febrile, pale, and edematous. The blood pressure was 100/50 mm. Hg, a loud, blowing diastolic murmur was audible along the left sternal border, and the spleen was palpable. Roentgenograms of the chest showed the heart to be much larger than it had been at the time of the last study (fig. 4).

At fluoroscopic examination, the metallic ring and cage of the Starr-Edwards valve were seen to move in a strikingly abnormal manner during

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**Figure 2**

Photographs of the heart of patient F. H. Left. The left ventricle, aortic valve “ring” and ascending aorta are shown. Only three or four sutures remain to fix the Starr-Edwards prosthesis to the necrotic annulus. The apex of the cage has burrowed into the wall of the ascending aorta forming a saccular aneurysm (An.). The Teflon tape, which was wrapped around the ascending aorta at the time of the operation, has burrowed through the aorta to form a part of the interior lining of this vessel. Thick scar tissue and numerous inflammatory cells are present in the periaortic area. Right. A close-up view of the aortic valve region. The prosthetic suture line is necrotic. L.V., left ventricle; M.V., anterior mitral leaflet; and P.T., pulmonary trunk.
the phases of the cardiac cycle. During systole, the valve tilted sharply forward and to the right, then returned to a normal position during diastole.

These motions of the valve were recorded by cineradiography, and also by means of serial biplane x-rays exposed at a rate of 6 per second.

**Figure 3**
The aortic root in patient F. H. The left photograph and middle photomicrograph are sections through the saccular aortic aneurysm formed by the cage of the Starr-Edwards prosthesis. The dotted line delineates the borders of the aneurysm. The area of attachment of the prosthesis is indicated. No elastic fibers were present in the wall of the saccular aortic aneurysm. Hematoxylin and eosin stain; × 2.2 (middle). The right photograph is a section through the aortic root, cut to include the anterior leaflet of the mitral valve (M.V.). A large abscess is present between the left atrial wall and the aortic valve ring, immediately beneath the area of attachment of the prosthesis. T.V., tricuspid valve; R.A., right atrium; V.S., ventricular septum.

**Figure 4**
Chest roentgenograms of patient W. L., illustrating changes in heart size before (A) and 10 months after (B) insertion of the Starr-Edwards aortic valve prosthesis. The appearance of the heart following the onset of severe aortic regurgitation secondary to the acute bacterial endocarditis is shown in C.
The positions of the valve during systole and diastole are shown in figure 5, and the motions of a normally functioning Starr-Edwards valve, recorded in another patient, are shown for comparison in figure 6.

After blood cultures had been obtained, the patient was empirically treated with total daily doses of penicillin (20 million units intravenously), streptomycin (2 Gm. intramuscularly), methicillin (4 Gm. intravenously), and chloramphenicol (2 Gm. intravenously). Each of five blood cultures subsequently grew Staph. albus, and in three of them Cytophaga anitratum (Herellea) was also found. In vitro, the Staph. albus was found sensitive to methicillin, and the C. anitratum to both chloramphenicol and streptomycin, and the initial therapeutic regimen was continued. The patient remained febrile, however, and became progressively more dyspneic. On his fifth hospital day, pulmonary edema and hypotension suddenly occurred, and the diastolic murmur, which had been consistently present, was no longer audible. At this time, a pulse was palpable in the right arm, but not in the left arm or legs. The lower half of the body became progressively cyanotic, and the patient died 1 hour later. A chest roentgenogram, obtained immediately after death, showed the prosthetic valve to be lying in the transverse aortic arch (fig. 7).

The appearance of the heart and aorta at autopsy (A64-189) is shown in figure 8. The prosthetic valve was found impacted in the aortic arch, completely occluding it immediately distal to the origin of the left carotid artery. The tissues of the aortic root, to which the valve had been sutured, were still attached to the Teflon ring of the valve. The entire area from which the valve had been dislodged was necrotic and ulcerated, and numerous Gram-positive cocci were evident histologically. An abscess was present in the periaortic area (fig. 9), and cultures of it grew hemolytic S. albus and Enterobacter.

**Discussion**

The clinical and pathologic findings in the three patients described would indicate that the inevitable consequence of infective endocarditis in a patient with a prosthetic aortic valve will be disruption of the valve from the aortic annulus. In each patient the development of bacterial endocarditis was shortly followed by evidences of progressively severe aortic regurgitation and death from cardiac
failure. At necropsy, the primary site of infection was found to be the tissues to which the prosthesis had been attached. The sutures fixing the valve were not broken, but had torn through the necrotic aortic annulus, and the valve was partially or completely detached. Although the wall of the aorta at the site of fixation of the valve was completely disrupted by the acute necrotizing infection, surrounding scar tissue prevented bleeding from the aortic lumen. The infectious process also involved the periaortic tissues, and acute abscesses and foci of necrosis were evident between the aorta and the walls of both right and left atria in each patient. In addition, in patient H. L., the infection extended into the mitral annulus; in patient W. L., to the tricuspid annulus via the membranous ventricular septum.

As noted above, aortic regurgitation and left heart failure, rather than the sequelae of infection, were the immediate causes of death in the patients described. In each of them the ominous progression of aortic regurgitation was appreciated, and replacement or reattachment of the infected prosthesis was considered. Such emergency operations were not undertaken, however, and the subsequent pathologic findings indicated that they would certainly have been fruitless. Dissection of the mediastinum, sufficient to permit cannulation and an aortotomy, would clearly have disseminated the infection in the periaortic tissues, and secure fixation of either the infected valve or a new one would also have proved impossible because of the necrotic tissues in the annulus. Thus, the experience with the present patients and, with one exception, the reports of others indicate that when infection becomes established at the site of a prosthetic aortic valve that it cannot be eradicated by antibiotics presently available. Also, since reoperation in such a patient is considered inadvisable, it would appear that major attention must be directed to prophylactic measures.

The application of meticulous aseptic techniques at the time of operation is, of course, the single most important factor in the prevention of postoperative infection, but in operations upon the heart and great vessels prophylactic antibiotics are also of proven value. In this clinic, daily doses of penicillin (2.4 million units) and streptomycin (1.0 Gm.) are given on the day before operation and for 1 week thereafter. With this regimen, and within the surgical environment of the Clinical Center, early postoperative endocarditis has not occurred in any of the more than 200 patients in whom prosthetic valves have been inserted. Accordingly, methicillin or other antibiotics are not given prophylactically, principally because of the increased risk of superinfection associated with their administration. Also, because of similar considerations, long-term penicillin administration, usually indicated in patients with rheumatic heart disease, is not given to patients with prosthetic valves.

In one of the present patients, W. L., staphylococcal endocarditis clearly resulted from dental extractions, even though he was
Figure 8

Photographs of the aorta and heart of patient W. L. Upper left. The ascending aorta is opened and the Starr-Edwards valve is lodged in the aortic arch. Tissue from the aortic valve "ring" is attached to the Teflon ring of the prosthesis. L.C., left carotid artery. Upper right. The detached prosthesis is viewed from the descending thoracic aorta (D.A.). Necrotic tissue is attached to the Teflon ring of the prosthesis. Lower left. The ascending aorta, aortic valve "ring," and left ventricle are opened. The site of the previous attachment of the prosthesis to the aortic root is totally necrotic. R.C., ostium of right coronary artery; L.C., ostium of left coronary artery. M.V., anterior mitral leaflet; L.V., left ventricle. Lower right. The right atrium (R.A.), tricuspid valve, and right ventricle (R.V.) are opened. The bulging membranous ventricular septum, which has become inflamed by direct extension of the infection from the aortic valve, is indicated by the dashed circle.
Photomicrographs of the aortic valve “ring” in patient W. L., showing the acute abscesses in the area between the aortic wall and the atria. The membranous septum (left) is inflamed and appears to be nearing perforation. The left section includes the aortic wall, right atrial (R.A.) wall, tricuspid valve (T.V.), and ventricular septum (V.S.). The right section includes the anterior leaflet of the mitral valve (M.V.) and the left atrial (L.A.) wall. There is considerable fibrous thickening of the mitral valve. Hematoxylin and eosin stains; × 2.2 in each.

Given prophylactic penicillin in doses similar to those recommended by the American Heart Association for patients with rheumatic heart disease.\textsuperscript{7} Patient H. L. also received penicillin before and after dental extractions but did not contract endocarditis at that time. Six months later, however, when he was edentulous and shortly after he had been fitted with dentures, he developed an ultimately fatal infection caused by \emph{beta hemolytic Streptococcus}. It is known that bacteremia can result from gingival ulcers caused by ill-fitting dentures,\textsuperscript{8} but one may only speculate as to whether this mechanism was responsible for endocarditis in this patient, and whether prophylactic penicillin would have been effective.

In a comprehensive study in this hospital by Rogosa and others,\textsuperscript{9} bacteremia was documented in more than 80 per cent of patients in whom either dental extractions or periodontal...
BACTERIAL ENDOCARDITIS

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Summary

The clinical and pathologic findings in three patients with prosthetic aortic valves are described. Each presented typical clinical features of acute bacterial endocarditis followed by the sudden development of severe and ultimately fatal aortic regurgitation. Pathologically the infectious process was characterized by extensive necrosis of the aortic annulus, disruption of the aortic wall, and the formation of abscesses in the periaortic tissues. In two patients the prosthetic valve was partially detached from the annulus, whereas in the other it was totally dislodged and impacted in the aortic arch shortly before death. In all, secondary operative intervention would have been fruitless because of the extent of the infection and the character of the tissue at the aortic root. In one patient fatal staphylococcal endocarditis followed dental extractions despite penicillin prophylaxis. A more comprehensive antibiotic regimen for patients with prosthetic cardiac valves is suggested.

References

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