Right-Sided Valvular Infective Endocarditis
A Clinicopathologic Study of Twelve Necropsy Patients

Clinical and necropsy features are described in twelve patients with infective endocarditis involving right-sided cardiac valves. In six patients infective endocarditis was limited to the tricuspid valve; in the other six vegetations also were present on one left-sided cardiac valve, but in only one of them was the infective endocarditis definitely primary on the left side of the heart. The tricuspid valve was the site of infective endocarditis in eleven patients and the pulmonic valve in one. The organisms responsible for the infective endocarditis were Staphylococcus aureus in six patients, Diplococcus pneumoniae in four, alpha Streptococcus in one, and Aspergillus flavus in one. Five patients were alcoholics, four were heroin addicts, two had blood dyscrasias, and one had congenital cardiac disease (ventricular septal defect). The infective endocarditis in each of the nine patients with alcoholism or heroin addiction and in the one with congenital heart disease was primary in the heart; in the remaining two patients, it was secondary to generalized infection affecting many body organs.

Acute pneumonia was a dominant clinical feature in ten of the twelve patients and appeared to be secondary to dislodgment of material from the right-sided cardiac vegetations. Six patients also had acute meningitis. Although the vegetations caused considerable damage to the right-sided cardiac valves, evidence of cardiac dysfunction was either absent or attributable to acute cor pulmonale secondary to the acute pneumonia. Attention is called to the common tetrad of chronic alcoholism, acute pneumonia, acute meningitis, and infective endocarditis. In nine of the twelve patients the right-sided vegetations did not extend to involve the basal attachments of the leaflets to the annuli. Thus, in these nine patients total excision of the valve leaflets would have eradicated their valvular endocarditis.

With the striking increase in heroin addiction in recent years, right-sided infective endocarditis has received considerable attention. Emphasis has been placed on the clinical features of right-sided infective endocarditis, and little attention has been given to the morphologic findings in infective endocarditis involving the tricuspid or pulmonic valves. We attempt to fill in this void by describing cardiac necropsy observations and relating them to clinical findings in twelve fatal cases of infective endocarditis involving right-sided cardiac valves.
RIGHT-SIDED VALVULAR INFECTIVE ENDOCARDITIS—ROBERTS, BUCHBINDER

**TABLE I Clinical and Necropsy Data in Twelve Patients with Right-Sided Infective Endocarditis (IE)**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr) and Sex</th>
<th>Valve(s) Involved</th>
<th>Causative Organism</th>
<th>Predisposing Factor</th>
<th>Acute Pneumonia</th>
<th>Acute Meningitis</th>
<th>Systolic Precordial Murmur and Intensity (0-6)</th>
<th>Diagnosis of IE During Life</th>
<th>Valve Dysfunction</th>
<th>Heart Failure</th>
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<tbody>
<tr>
<td>1</td>
<td>64,M</td>
<td>TV</td>
<td>Staph. aureus*</td>
<td>Lymphoma</td>
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<td>0</td>
<td>(3/6)</td>
<td>TR</td>
<td>+</td>
<td>+</td>
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<tr>
<td>2</td>
<td>31,F</td>
<td>TV</td>
<td>Staph. aureus</td>
<td>H</td>
<td>+</td>
<td>0</td>
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<td>TR</td>
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<td>TV</td>
<td>D. pneumoniae</td>
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<td>+</td>
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<tr>
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<td>+</td>
<td>0</td>
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<td>TR</td>
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<td>+</td>
</tr>
<tr>
<td>5</td>
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<td>H</td>
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<td>+</td>
<td>(2/6)</td>
<td>TR</td>
<td>+</td>
<td>+</td>
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<td>A. flavus*</td>
<td>Thymic dysplasia</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>9</td>
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<td>A</td>
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<td>0</td>
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<td>A</td>
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<td>0</td>
<td>(5/6)</td>
<td>AR</td>
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</table>

NOTE: A = alcoholism; AR = aortic regurgitation; AV = aortic valve; CA = coronary artery; CHF = congestive heart failure; GN = glomerulonephritis; H = heroin addiction; IE = infective endocarditis; MV = mitral valve; PR = pulmonic regurgitation; PV = pulmonic valve; TR = tricuspid regurgitation; TS = tricuspid stenosis; TV = tricuspid valve.

* IE secondary to generalized sepsis.
† Represent minimum duration.

**PATIENTS STUDIED**

Among fifty-seven patients with fatal active valvular infective endocarditis studied at necropsy by us, forty-five had vegetations limited to the left side of the heart [1], and twelve had vegetations involving one right-sided cardiac valve. Certain clinical and necropsy observations in the latter twelve patients are summarized in Table I. Their ages ranged from ten months to sixty-five years; eight were male, and four were female. In six, vegetations were confined to the tricuspid valve; in the other six, vegetations involved one left-sided cardiac valve in addition to the tricuspid (five patients) or pulmonic valve (one patient). Blood cultures, obtained in eleven patients, were positive in each: Staph. aureus in six, D. pneumoniae in three, alpha Streptococcus in one and Aspergillus flavus in one. Culture of cerebrospinal fluid in the twelfth patient yielded D. pneumoniae, and histologic study of his vegetations at necropsy showed gram-positive diplococci. Nine patients were either alcoholics (five patients) or heroin addicts (4 patients), two others had altered defense mechanisms (Hodgkin’s disease in one and thymic dysplasia in one) and one had congenital cardiac disease (ventricular septal defect). Four of the five alcoholics had pneumonia; each of the other three patients (Cases 10, 11 and 12) had both right- and left-sided congestive cardiac failure secondary to endocarditis, causing regurgitation of one left-sided cardiac valve in two patients and a left ventricular-right atrial shunt in one (Case 11).

Precordial murmurs were heard in nine of the twelve patients. All nine had systolic murmurs, and three of them (Cases 10, 11 and 12) had diastolic murmurs (from destruction of aortic valves by infection). Four of six patients with endocarditis limited to the tricuspid valve had systolic murmurs, but in only one did the murmur get louder with inspiration. In one patient (Case 11) whose membranous ventricular septum was ruptured by the infective process, a continuous precordial murmur developed several days before his death, and clinically a diagnosis of acquired ventricular septal defect was made. All twelve patients had fever (oral temperature more than 100°F). The spleen was palpated in three patients, fundal hemorrhages were observed in two, and one had dermal petechiae. The diagnosis of infective endocarditis was made during life in only three of the six patients with isolated tricuspid valve endocarditis and in only two of six with...
Right-Sided Valvular Infective Endocarditis—Roberts, Buchbinder

<table>
<thead>
<tr>
<th>Duration of IE (days)</th>
<th>Principal Causes of Death</th>
<th>Heart Weight (gm)</th>
<th>Ruptured TV Chordae Tendineae</th>
<th>Bacteria in TV or PV</th>
<th>Papillary Muscle Necrosis</th>
<th>Myocarditis</th>
<th>Renal Abnormalities</th>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>Septic infarcts</td>
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† Spleen palpated clinically.
§ Patient had systemic hypertension.
‡ Diastolic murmur of aortic regurgitation present also.
# Operatively excised in distant past.

Combined right- and left-sided endocarditis. Eleven patients received antibiotics: eight received a drug appropriate for the causative organism, three a questionably appropriate antibiotic and one an inappropriate drug.

All valves were functionally normal before they became the sites of active infective endocarditis. Infective endocarditis caused valve dysfunction in seven patients regurgitation in six (tricuspid valve three, aortic valve three) and possible tricuspid stenosis in one. Each of these seven patients had right- (four patients) or left-sided (three patients) cardiac failure. Congestive heart failure was the principal cause of death, however, in only three patients, and each of them had aortic regurgitation. In the remaining nine patients in whom congestive cardiac failure was either not present (five patients) or of secondary importance (four patients), the principal cause of death was related to extracardiac abnormalities: acute pneumonia, acute meningitis, generalized infection, renal failure or combinations of these. Acute pneumonia was the most common factor, occurring in ten of the twelve patients, and the two without pneumonia had either single or small flat tricuspid valve vegetations.

Necropsy findings

Certain necropsy findings are summarized in Table I and illustrated in Figures 1 through 12. Vegetations were present on twenty-four of the thirty-three tricuspid valve leaflets; five patients had vegetations on all three leaflets, three on two leaflets and three on only one leaflet. Each of the three patients with only one tricuspid valve leaflet involved also had infective endocarditis involving one or both left-sided cardiac valves. Six of the eight patients with vegetations on two or more tricuspid valve cusps had infective endocarditis limited to the right side of the heart; the seventh patient (Case 11) had left-sided involvement only because of extension of the tricuspid valve infection through the membranous ventricular septum to the base of one aortic valve cusp; the eighth patient had vegetations on all three tricuspid valve cusps and only a minute vegetation on one of the three aortic valve cusps. In the latter patient, therefore, the left-sided infection is considered secondary to the one patient (Case 12) each of the twenty valves containing vegetations appeared to be anatomically normal at sites not involved by the infection. The aortic valve in this patient (Case 12), who also had a small ventricular septal defect, consisted of three distinctly unequal sized cusps, but none was thickened, and the valve almost certainly functioned normally before it became infected. Thus, the infective endocarditis in eleven of the twelve patients involved previously anatomically normal valves.

Of the eleven patients with infective endocarditis involving the tricuspid valve vegetations were present on twenty-four of the thirty-three tricuspid valve leaflets; five patients had vegetations on all three leaflets, three on two leaflets and three on only one leaflet. Each of the three patients with only one tricuspid valve leaflet involved also had infective endocarditis involving one or both left-sided cardiac valves. Six of the eight patients with vegetations on two or more tricuspid valve cusps had infective endocarditis limited to the right side of the heart; the seventh patient (Case 11) had left-sided involvement only because of extension of the tricuspid valve infection through the membranous ventricular septum to the base of one aortic valve cusp; the eighth patient had vegetations on all three tricuspid valve cusps and only a minute vegetation on one of the three aortic valve cusps. In the latter patient, therefore, the left-sided infection is considered secondary to the
Figure 1. Case 2. Staphylococcus aureus endocarditis of tricuspid valve in a thirty-one year old female heroin addict (A67-257). Acute pneumonia developed, probably from septic emboli, about thirty-five days before death. Pulmonary abscesses were seen on the chest roentgenogram when she was hospitalized thirteen days before death. A grade 3/6 blowing precordial systolic murmur was audible and the liver was pulsatile. She died of congestive heart failure and renal failure. "Focal embolic" glomerulonephritis was found at necropsy. a, tricuspid valve viewed from right ventricle showing vegetations on each leaflet. b, opened right heart showing vegetations on each tricuspid valve cusp. c, close-up of bracketed area in b showing several ruptured chordae tendineae. d, photomicrograph of section through right atrium, right ventricle and tricuspid valve leaflet. Hematoxylin and eosin stain; original magnification X 5, reduced by 28 per cent. e, high power view of bracketed area in d. Vegetation consists of numerous polymorphonuclear leukocytes enmeshed in a fibrin network. Darkly stained areas are colonies of gram-positive cocci. Hematoxylin and eosin stain; original magnification X 108, reduced by 28 per cent.

Figure 2. Case 3. Tricuspid valve pneumococcal endocarditis in a sixty-five year old alcoholic (A68-101) with evidence of cardiac infection for about 112 days. a, in this view a recent vegetation is partially enclosed by dashes. A perforation is present also in the leaflet. b, longitudinal section of the vegetation shown in a. The vegetation contains calcific deposits. c, histologic section of vegetation which contained fibrin and inflammatory cells but no stainable organisms. Elastic van Gieson stain; original magnification X 3, reduced by 25 per cent.
Figure 3. Case 4. Staphylococcus aureus endocarditis of tricuspid valve (A70-140). a, tricuspid valve viewed from right atrium. b, same valve viewed from right ventricle. c, view of opened right atrium, tricuspid valve and right ventricle. d, histologic section of vegetation which involves the distal half of the anterior tricuspid leaflet. Movat stain; original magnification X 4, reduced by 30 per cent.

Figure 4. Case 5. Chest roentgenograms taken on dates shown (A70-87). Patient died of pulmonary infection on March 17, 1970.

Figure 5. Case 5. Staphylococcus aureus endocarditis of tricuspid valve in a thirty-five year old female heroin addict whose chest roentgenograms are shown in Figure 4. She had been well until about one week before death when "acute pneumonia" developed. About three days before death, she suffered from headache and stiff neck. When hospitalized several hours before death, in addition to evidence of acute pneumonia, probably from septic emboli, and acute meningitis, she had a grade 2/6 precordial systolic murmur, which increased with inspiration, and a pulsatile liver. a, tricuspid valve viewed from right atrium. The orifice appears to be narrowed by the vegetation. b, tricuspid valve viewed from right ventricle. c, view of opened tricuspid valve. d, section of right lung showing infarct caused by septic embolus in right pulmonary artery. e, photomicrograph of portion of tricuspid valve vegetation. Dark staining areas in the leaflet represent gram-positive cocci. The surface of the vegetation is relatively smooth. Movat stain; original magnification X 5, reduced by 17 per cent.
right-sided one. The number of vegetations on the tricuspid leaflets varied from one (in three patients) to innumerable (in Case 5). The number of vegetations on the tricuspid valve leaflets in the remaining seven patients varied from two to five. The individual vegetations on the tricuspid valve varied from 0.1 to 5 cm in largest diameter. The largest single vegetation occurred in Case 5, and although it appeared to obstruct the valvular orifice it was attached entirely to the anterior leaflet. The next largest occurred in a patient with fungal endocarditis (Case 8). The tricuspid valve vegetations involved the basal attachments of the leaflets, i.e., the annulus, in three patients, but in only one of them (Case 11) did it actually extend into the annulus and cause a ring abscess. Thus, excision of the leaflets would have totally removed the tricuspid valve vegetations in eight of the eleven patients. The shapes of the tricuspid valve vegetations in six patients were relatively flat and in the other five fungating. The surfaces of most vegetations were relatively smooth in seven patients and relatively rough in the other four. The vegetations caused rupture of several chordae tendineae in five patients, all of whom had multiple and usually large vegetations; in the other six without ruptured chordae the vegetations were either single or small. In none of the eleven patients did the vegetations cause gross disappearance of leaflet tissue either by perforation or by dissolution of a portion of tricuspid leaflet.

On histologic examination, organisms were observed in tricuspid valve vegetations in seven of the eleven patients. Polymorphonuclear leukocytes were observed in the vegetations in all eleven patients; in eight abscesses were present. In three patients the inflammatory process and organisms were found in the central portions of the leaflets with preservation of cuspal tissue peripherally. In four other patients, distal portions of leaflet were completely destroyed, being incorporated into the inflammatory process; in three other patients the inflammatory process was superimposed on the surface of the tricuspid leaflets with good preservation of the underlying cusp. Calcific deposits were present in one tricuspid valve (Case 3), but this patient had had clinical evidence of infective endocarditis for at least 112 days.
Figure 8. Case 8. Fungal endocarditis in a ten month old boy with a generalized infection involving many body organs (A70-78). Single large vegetations (dashed circles) were present on the tricuspid (a and b) and mitral (c and d) valves. A large myocardial abscess is designated by the closed circle in c and d.

The infection involving the pulmonic valve in one patient consisted of a single flat, relatively rough-surfaced vegetation involving two cusps and the intervening commissure. The vegetation produced a large tear in one cusp, almost surely producing pulmonic regurgitation. The infective process extended to the margin of attachment of one cusp. On histologic study, the involved pulmonic cusps contained large collections of polymorphonuclear leukocytes, and both surfaces were covered by fibrin. Organisms were not found in the involved pulmonic cusps.

Mural vegetations were present in three patients. In two they were located on the right ventricular endocardium: in one (Case 3) from contact with the free swinging anterior tricuspid leaflet (since its chordae were ruptured), and in one (Case 12) on a mural jet lesion produced earlier by congenital ventricular septal defect. In the third patient (Case 5) vegetative material was located on the right atrial endocardium and was due to contact of a large tricuspid valve vegetation.

On gross examination, distinct lesions were observed in myocardial walls in only two of the twelve patients: one (Case 8) had well circumscribed abscesses in the left ventricular free wall; the other (Case 9) had extensive, less well circumscribed foci of inflammatory necrosis in both left ventricular papillary muscles and a focus of acellular necrosis in the left ventricular free wall. On examination of 100 separate histologic sec-
tions of cardiac wall (five to fourteen per patient [average 9]) including sections of at least two of the three major papillary muscles of each heart, focal myocardial lesions were observed in the hearts of four patients. Three patients (Cases 1, 8 and 9) had myocardial abscesses. In the latter two patients (Cases 8 and 9), as already mentioned, they were large enough to be visible grossly; in the third (Case 1) only one minute myocardial abscess, containing colonies of bacteria, was observed on examination of eight large [2] sections of myocardial wall. Colonies of organisms also were observed in the myocardial abscesses in two patients (Cases 8 and 9), in both of whom septic emboli were observed in one or more coronary arteries (extramural in Case 9, intramural in Case 8). A minute focus of acute inflammatory cells also was observed in one patient (Case 11), but the cells were present in fibrous tissue, not in myocardium, in the distal portion of one papillary muscle. Only three patients had foci of myocardial necrosis, and two of them had coronary arterial emboli. The foci of necrosis in all three were located in both left ventricular papillary muscles, and two also had foci of necrosis in the left ventricular free wall. None of the other nine patients had papillary muscle necrosis, and none of the twelve had necrosis of the anterior papillary muscle of the right ventricle. The necrosis in one patient (Case 8) was associated with extensive dystrophic calcification of individual myocardial fibers. In another patient (Case 11) calcific deposits also were found in several individual myocardial fibers. Except for microscopic-sized foci in the apices of the left ventricular papillary muscles in several patients, no interstitial or replacement myocardial fibrosis was observed.

At necropsy, acute pneumonia with pulmonary infarcts was found in ten of the twelve patients, and seven had pulmonary abscesses. Material similar to that forming the right-sided cardiac vegetations was found in pulmonary arteries in

Figure 10. Case 10. Pneumococcal endocarditis involving tricuspid (a) and aortic (b) valves in a fifty-eight year old alcoholic (DCGH No. 71A-14). The vegetation on the tricuspid valve is small, whereas the vegetations on the aortic valve are large and cause extensive destruction of the cusps. c, histologic section of a portion of tricuspid leaflet showing abscess formation. Hematoxylin and eosin stain; original magnification X 16, reduced by 33 per cent.

Figure 11. Diagrammatic representation of development of aortic regurgitation and left to right shunt in a fifty-five year old man (WHC No. A70-155) with pneumococcal endocarditis and alcoholism. He noted fever, cough, and neck and knee pain twenty-six days before death. Overt signs of acute meningitis were present at the time of hospitalization nineteen days before death. Subsequently a murmur and signs of aortic regurgitation developed, and after that a "continuous murmur" due to the aortico-right atrial fistula. Death was due to intractable heart failure. (1) Normal cardiac anatomy. (2) Initial nidus of infection on tricuspid valve leaflet. (3) Extension of tricuspid vegetation through membranous portion of ventricular septum onto one of three aortic valve cusps. (4) Consequent perforation of aortic valve cusp causing aortic regurgitation and rupture of the membranous ventricular septum causing a left ventricular-right atrial fistula.
seven of the ten patients with pneumonia, strongly suggesting that the pneumonia was secondary to dislodgment of vegetative material into the pulmonary circulation.

COMMENTS

Certain facts regarding right-sided infective endocarditis have emerged from review of previous reports on this subject and from study of our patients: (1) Its frequency is far less than left-sided infective endocarditis. It composes about 10 per cent of all cases of infective endocarditis. (2) It is usually caused by highly virulent or unusual organisms, the Staphylococcus being the most common. (3) The involved right-sided valve is, with rare exception, anatomically and functionally normal before the onset of infective endocarditis. (4) A predisposing factor is nearly always apparent. The most frequent ones are opiate addiction; alcoholism; generalized infections in patients with immunologic deficiencies, particularly lymphoma; congenital cardiac disease and dermal infections, particularly in young children or infants, with subsequent septicemia. (5) Diagnosis is difficult since the predominant clinical features are extracardiac, mainly, acute pneumonia; precordial murmurs are frequently absent or if present are soft and atypically located, and evidences of congestive cardiac failure are absent or if present rarely prominent.

The infrequency of right-sided infective endocarditis compared to the relative frequency of left-sided infective endocarditis has been explained by the lower pressure in the right side of the heart [3]. If the difference in pressure on the two sides of the heart is the major factor, the ratio between the frequency of right-sided to left-sided infective endocarditis might be expected to approximate the ratio between the peak systolic pressure in the right ventricle and that in the left ventricle.

Figure 12. Alpha hemolytic Streptococcus endocarditis in a five year old girl (A69-260) with congenital ventricular septal defect (VSD). Pneumonia and anemia developed four months before death, and two months later a grade 2/6 murmur of aortic regurgitation was noted for the first time. Death resulted from a large brain embolus. Vegetation probably formed initially on the jet lesion in the right ventricular outflow tract. Dislodgment of portions of right ventricular vegetation produced septic pulmonary emboli which presented clinically as "acute pneumonia." The exact mechanism of involvement of the aortic valve by the infective process is uncertain. a, diagrammatic representation of location of vegetative material. Calcific deposits developed in aortic valve vegetation during the four month course. RA = right atrium; RV = right ventricle; PT = pulmonary trunk; LA = left atrium; A = aneurysm with orifice just below aortic valve. b, view of opened right atrium, tricuspid valve and right ventricle showing the large vegetation (enclosed by dashed line) in the right ventricular outflow tract adjacent to the small ventricular septal defect. c, view of opened left ventricle, aortic valve and aorta showing partial but extensive destruction of aortic valve cusps by vegetative material. The borders of the ventricular septal defect are free of vegetation. d, photomicrograph of section through the ventricular septal defect including a portion of aorta, aortic valve (A.V.) cusp and ventricular septum (V.S.). The endocardium bordering the ventricular septal defect and that in the right ventricular outflow tract is very thick. C.A.-coronary artery. Elastic van Gieson stain; original magnification X 8, reduced by 15 per cent.
and indeed this is the case. The peak ventricular systolic pressure normally is about one sixth or 17 per cent of the peak left ventricular systolic pressure, and in at least 10 per cent of all cases of infective endocarditis the right-sided valves are involved. Thus, these figures of 10 and 17 per cent are sufficiently close to one another to allow this pressure explanation to be extremely plausible. Another factor mentioned as explaining the much lower frequency of right-sided infective endocarditis is lack of underlying disease of the right-sided cardiac valves compared to that involving the left-sided valves. In our study [1] of forty-five necropsy patients with active valvular infective endocarditis limited to the left side of the heart, there was evidence that the valve had been anatomically abnormal before the onset of infective endocarditis in 47 per cent whereas there was no evidence of previous right-sided valvar disease in any of our patients with right-sided infective endocarditis. The increased susceptibility of previously abnormal valves to infective endocarditis is well established, and this factor may be the second most important one in explaining the higher frequency of left-sided infective endocarditis. Whether or not the lower oxygen tension of the blood in the right side of the heart is important (by discouraging growth of aerobic bacteria) is uncertain.

Most studies [4-18], including ours, show that right-sided cardiac valves are usually attacked by highly virulent and unusual organisms. Of the twenty-three necropsy patients with right-sided (two had pulmonary arterial endarteritis from patent ductus arteriosus) infective endocarditis observed at the Mayo Clinic from 1910 to 1955 and described by Bain et al. [11] in 1958, the offending organism was identified in nineteen: Staphylococcus was responsible in eleven (58 per cent), Pneumococcus in three (18 per cent), Streptococcus in ten (53 per cent), miscellaneous in two, and Gonococcus in one (5 per cent). In contrast, of Thayer's total 536 cases of infective endocarditis described in 1931 [5], Staph. aureus was responsible in only 7 per cent, Pneumococcus in 15 per cent, Streptococcus in 63 per cent and Gonococcus in 11 per cent. Of 100 patients with infective endocarditis acquired outside the hospital between 1956 and 1965 [19], Staphylococcus was responsible in twenty-three, Streptococcus in fifty-six (viridans in twenty-seven), miscellaneous in seven (but none had Pneumococcus or Gonococcus) and negative in fourteen. Studies in opiate addicts [7-10,13-18] have shown an even greater propensity for the Staphylococcus to be the cause of right-sided infective endocarditis. A review of forty-eight cases (69 per cent fatal) of infective endocarditis in opiate addicts by Louria et al. [14] disclosed that the offending organism was Staphylococcus (aureus in thirteen, epidermidis in two) in fifteen of the sixteen patients with right-sided endocarditis (tricuspid valve in each). Among sixty-two fatal cases of infective endocarditis in opiate addicts reviewed by Sapira [16] in 1968, Staph. aureus was the offending organism in nine of thirteen with isolated right-sided cardiac vegetations, whereas it was responsible in only six of forty-six patients with isolated left-sided infective endocarditis (organism unknown in thirteen). Of sixteen opiate addicts with infective endocarditis described in 1970 by Ramsey et al. [18], Staph. aureus was the cause in three of the four patients with right-sided (tricuspid) infective endocarditis in whom the organism was known but in only one of twelve patients with isolated left-sided infective endocarditis. Staph. aureus also was the cause of the right-sided infective endocarditis in each of four heroin addicts described herein but was responsible for infective endocarditis in only one of the remaining eight patients. Although it usually attacks previously normal right-sided cardiac valves, Staphylococcus is commonly the offending organism in patients with infective endocarditis complicating congenital cardiovascular malformations. Of thirty-eight patients with infective endocarditis and congenital heart disease (twenty-three had ventricular septal defect) described by Vogler and Dorney [20], Staphylococcus was responsible for the infection in thirteen (41 per cent) and alpha Streptococcus in nine (28 per cent) of the thirty-two patients in whom the organism was known.

In none of the multiple papers concerning right-or left-sided infective endocarditis in opiate addicts has Pneumococcus been mentioned as the offending organism. In four of our twelve patients with right-sided infective endocarditis, D. pneumonae was the offending bacterium. Each of these patients was a chronic alcoholic and three also had meningitis. In the pre-heroin-addiction era, however, Pneumococcus was recognized as a frequent cause of right-sided infective endocarditis. Of twenty cases of infective endocarditis involving the tricuspid valve reported before 1940 [6], none (45 per cent) were caused by Pneumococcus. Of a total of 584 patients with infective endocarditis subjected to necropsy at the Philadelphia General Hospital from 1920 to 1940, only eleven (2 per cent) had infective endocarditis restricted to the tricuspid valve, but of the sixty-two cases of endocarditis the tricuspid valve alone was involved in nine (15 per cent) [6]. Even earlier, in 1904, Preble [4] in reviewing 141 cases of pneumococcal endocarditis showed that in 18 per cent there were vegetations on right-
sided cardiac valves, whereas infective endocarditis due to organisms other than Pneumococcus caused right-sided vegetations in only 7 per cent of the cases. Preble also mentioned alcoholism, as well as malnutrition, as a predisposing factor to pneumococcal endocarditis, and he also stressed the frequent association of pneumococcal infective endocarditis with meningitis and pneumonia. He found that 60 per cent of patients with pneumococcal endocarditis had meningitis and that 30 per cent of patients with pneumococcal meningitis had endocarditis. Goldburgh et al. [6] found pneumococcal endocarditis in 5 per cent of the patients who died with lobar pneumonia. Although Pneumococcus was the offending organism in 15 per cent of Thayer’s 536 patients with infective endocarditis described before 1931 [5], since the introduction of antibiotics it has caused less than 3 per cent of the cases of infective endocarditis [21]. Of fifteen patients (ten fatal) with pneumococcal endocarditis studied at the Cincinnati General Hospital from 1945 to 1965, three had vegetations limited to the tricuspid valve (the other twelve had either mitral or aortic vegetations) [21]. Thirteen of the fifteen patients also had meningitis.

Although heroin addiction is now a well recognized predisposing factor to infective endocarditis on either side of the heart, the frequency of alcoholism as a predisposing factor to right-sided infective endocarditis apparently is not well appreciated. Congenital cardiac disease is a well recognized predisposing factor to infective endocarditis [20,22-24]. In this circumstance the right-sided vegetations are most frequently observed in patients with small ventricular septal defects and left to right shunts through them as in our Case 12. The resulting vegetations, however, most often occur on the thickened right ventricular mural endocardium rather than on valvular (tricuspid) endocardium, but both were involved in our patient. Persistent patent ductus arteriosus also may be complicated by vegetations occurring on the pulmonary arterial side of the left to right shunt. Strictly speaking, however, vegetations involving the ductus or pulmonary artery represent endarteritis and not endocarditis. Infective endocarditis complicating previously stenotic tricuspid or pulmonic valves is uncommon. Rheumatic tricuspid valve disease is always accompanied by rheumatic mitral stenosis and frequently also by aortic valvular involvement [25]. Infective endocarditis involving hearts with previously diseased left- and right-sided valves nearly always attacks only one or both left-sided valves and spares the right-sided valves. Infective endocarditis, however, rarely attacks hearts with previous three- or four-valve involvement anyway, possibly because the left-sided valves in this circumstance are usually heavily calcified and stenotic, and superimposition of infective endocarditis on heavily calcified valves is uncommon. Furthermore, involvement of congenitally malformed, particularly stenotic, pulmonic valves is infrequent, although several patients with congenital pulmonic stenosis and infective endocarditis have been described [20,22-24].

Although the diagnosis of left-sided infective endocarditis is usually established during life, the diagnosis of right sided infective endocarditis is far more difficult to make and often is not even suspected during life. The major reason is because the latter illness is dominated by extracardiac signs and symptoms. Acute pneumonia is the usual presenting feature of right-sided infective endocarditis, occurring in ten of our twelve patients, and it dominates the clinical course. The pneumonia is usually embolic in origin, resulting from dislodgment of vegetative material from the right-sided cardiac vegetations. Acute meningitis also may occur and be the dominant feature. Signs of right-sided congestive cardiac failure may be absent or minimal or, if present, readily explainable as secondary to acute cor pulmonale from the acute pneumonia. Precordial murmurs may be absent entirely and, if present, may be soft, atypically located and may not increase in intensity with inspiration. Since fever and anemia are common, the precardial murmurs may be dismissed as being "hemic" in origin. Cardiomegaly, distention of jugular veins and pulsation of the liver are often not observed in patients with right-sided infective endocarditis. Death in patients with isolated right-sided infective endocarditis usually can be attributed to the extracardiac manifestations, usually pneumonia. In none of our six patients with isolated right-sided infective endocarditis was congestive cardiac failure an important factor. Furthermore, in only two of the six patients with infective endocarditis involving both right- and left-sided cardiac valves was congestive cardiac failure a major manifestation of the illness, and in both infective endocarditis caused severe aortic regurgitation.

A number of papers have been published on right-sided infective endocarditis, but none have emphasized the cardiac-pathologic features of this condition, and few have even illustrated its morphologic aspects. Of our twelve patients, infective endocarditis was definitely primary on the right side of the heart in nine; in six of these no left-sided vegetations were present, and in the other three the right-sided vegetations were large or extensive, and the left-sided vegetations were minute or smaller. Dislodgment of organisms from the
intimated lungs into the pulmonary veins may be the mechanism responsible for the left-sided vegetations. In two other patients single similar-sized vegetations were located on both tricuspid and mitral valves and therefore which one came first is uncertain; both patients had generalized infection involving several body organs. In one of the twelve patients large vegetations destroyed the aortic valve, and only one small vegetation was present on the right side of the heart. Thus, this patient (Case 10) appears to be the only one in whom the right-sided infective endocarditis was definitely secondary to left-sided infective endocarditis.

Vegetations on the tricuspid valve may be similar in appearance to those involving the mitral valve. Rupture of chordae tendineae is common, occurring in five of our eleven patients with tricuspid valve vegetations. Unlike rupture of chordae tendineae of the mitral valve, which virtually always leads to severe mitral regurgitation [26], rupture of tricuspid valvular chordae may produce no clinical evidence of tricuspid regurgitation since normally the pressures in the right ventricle and right atrium are low and not markedly different. When evidence of tricuspid regurgitation is present in patients with infective endocarditis involving this valve, it is probable that the elevation in right ventricular pressure is a consequence of extensive acute pneumonia and acute cor pulmonale. Perforation or disappearance of tricuspid leaflet tissue occurred in none of our eleven patients despite highly virulent organisms. Again, this difference may be explained by the lower pressure on the right side of the heart which may decrease the rate of valve destruction by the infective process. Another factor may be the duration of illness which is shorter in patients with right-sided infective endocarditis as compared to patients with isolated left-sided infective endocarditis. Possibly the former patients die of widespread pneumonia before the right-sided vegetations have had time to destroy the valves more extensively.

From study of our twelve patients and from reports of others of right-sided infective endocarditis [4-18,20-24,27-30], it appears that the tricuspid valve is far more prone to be the site of vegetations than is the pulmonic valve. Only one of our twelve patients had pulmonic valve vegetations, and he also had mitral valve infective endocarditis. Pulmonic valve vegetations were present in only one of the twelve fatal cases of isolated right-sided infective endocarditis reported by Sapira [16]. In contrast, infective endocarditis on the left side involves the semilunar (aortic) valve more frequently than the atrioventricular (mitral) valve [1]. Fungating vegetations on the pulmonic valve also appear to be infrequent as contrasted to their frequency on the aortic valve. In none of our twelve patients with infective endocarditis were both right-sided cardiac valves involved, whereas involvement of both left-sided cardiac valves by infective endocarditis is common. This difference results from several factors. Although pulmonic regurgitation may result from infective endocarditis involving this valve, the amount of regurgitation is usually small since the valve usually is not extensively damaged and the pulmonary pressure is relatively low. In contrast, vegetations on the aortic valve are usually larger and frequently severely damage the cusps with resultant marked regurgitation. Also, the higher aortic diastolic pressure may dislodge the aortic valves and cause them to attach to mitral leaflets or chordae. The pulmonary arterial pressure may not be high enough to dislodge the pulmonic valve vegetations retrogradely. Also, the pulmonic valve is separated from the tricuspid valve by myocardium (crista supraventricularis), whereas the anterior mitral leaflet is continuous with the aortic valve.

Although myocardial lesions are frequent in patients with infective endocarditis involving one or both left-sided cardiac valves, they are usually absent in patients with isolated right-sided infective endocarditis. Only one of our six patients with isolated right-sided infective endocarditis had myocardial lesions and he had widespread abscesses in many body organs. Two of our six patients with combined right- and left-sided infective endocarditis had myocardial foci of inflammation, and in each coronary arterial septic emboli were the explanation.

Recently, total valve excision has been employed as therapy for patients with right-sided infective endocarditis unresponsive to antibiotic therapy [31]. In nine of our eleven patients with tricuspid valve infective endocarditis, the vegetations did not extend to the basal attachments of the leaflets. Therefore, total excision of the tricuspid valves would have eradicated the right-sided infective endocarditis. In only one of the two patients in whom the infective process extended to the level of the basal attachment of a tricuspid leaflet did it actually burrow into the annulus to cause a ring abscess. Even though the infective endocarditis may have extended to the level of the valve annulus, this would not necessarily preclude total valve excision and successful outcome because valve excision may serve simply to eradicate the source of septic emboli to the lungs which cause infarction, pneumonia and abscess-
es, and the pulmonary infection is the major cause of death in these patients. Although man
cay tolerate total excision of either the tricuspid or pulmonic valve without symptomatic evidence
of cardiac dysfunction, if both valves become in-
competent, or if one becomes stenotic and the
other incompetent, cardiac decompensation is the
result. An ideal way to produce severe congestive
heart failure in animals is to incise or excise the
tricuspid valve causing incompetency and banding
the pulmonary trunk causing stenosis [32].

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