

Infective Endocarditis Due to Anaerobic and Microaerophilic Bacteria

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Seven cases of infective endocarditis (IE) due to anaerobic or microaerophilic bacteria were seen in a period of 42 months at Rancho Los Amigos Hospital (Downey, California), representing 10.6 percent of the total number of 66 cases that carried the diagnosis of IE. Five of the 66 patients had polymicrobial endocarditis. Three of five patients with polymicrobial endocarditis had at least one anaerobic or microaerophilic microorganism isolated from the blood, and all five patients practiced intravenous drug abuse. Six of the seven patients with anaerobic or microaerophilic IE were women. The three patients who had anaerobic Gram-negative bacillary endocarditis were drug abusers. None of the isolated organisms were Bacteroides fragilis. The following heart valves were involved in the seven patients with anaerobic or microaerophilic IE: tricuspid (three), mitral (two), aortic (one) and tricuspid plus aortic (one). Three of the seven patients had preexistent valvular disease, and two required tricuspid valvectomy. Only one patient had serious systemic embolism (cerebral), but all four drug abusers had septic pulmonary embolism. All seven patients recovered with appropriate antimicrobial therapy.

INFECTIVE ENDOCARDITIS (IE) due to anaerobic and microaerophilic microorganisms has been considered a relatively uncommon condition. In 1970 Felner and Dowell¹ from the Centers for Disease Control reviewed anaerobic bacterial endocarditis and reported an incidence of 1.3 percent from the literature. In 1977 Pelletier and Petersdorf² reviewed 125 cases of IE seen at the University of Washington Hospitals and reported three cases of endocarditis due to microaerophilic streptococci

and five cases due to strict anaerobes (6.4 percent of total). Their review showed a 9.6 percent incidence of cases with negative cultures. More recently von Reyn and co-workers³ reported a 7.7 percent incidence of anaerobic or microaerophilic IE in 123 total cases, with a 5.5 percent incidence of cases with negative cultures.

At Rancho Los Amigos Hospital, we have recently seen seven cases of IE due to anaerobic or microaerophilic bacteria. We have reviewed the clinical characteristics of this disease in these seven patients to gain a clearer understanding of the clinical features associated with it. We have also reviewed our experience with infective endocarditis to determine whether the incidence of endocarditis

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ABBREVIATIONS USED IN TEXT
 IE= infective endocarditis
 TSB= trypticase soy broth

due to these particular microorganisms differs from that observed by others.

Patients and Methods

A list of patients discharged from January 1977 to June 1980 with a diagnosis of infective endocarditis was obtained from the medical records department of the Rancho Los Amigos Hospital. Criteria used for establishing the diagnosis of IE were as previously described.³ To be included in the general survey, patients had to meet the minimal criteria set for the diagnosis of "possible endocarditis." The charts were reviewed for general patient data and to determine which patients had IE due to anaerobic or microaerophilic bacteria. These latter charts were then analyzed in detail and various clinical characteristics were tabulated and evaluated retrospectively. The patients included in this study were seen by one or both of the authors during their admission for IE.

In our hospital the usual procedure for doing blood cultures was to inject 10 ml of blood into each of a two-bottle set of broth culture media. One bottle contained 9 ml of trypticase soy broth (TSB, Clinical Standards, Carson, Calif.) and the other 90 ml of thioglycolate broth (Thio, Clinical Standards). Each of these bottles contained 0.025 percent of sodium polyanethol sulfonate (SPS). Inoculated bottles of TSB were immediately vented by aseptically inserting sterile, cotton-plugged airway needles. Broth bottles were incubated at 35°C for at least seven days. Aliquot specimens from the bottles were taken for subculture on the first, third and fifth day if no growth was seen. Microbiologic isolation and identification were carried out by conventional methods.⁴⁻⁶

Results

From January 1977 to June 1980 66 patients were discharged from Rancho Los Amigos Hospital with a diagnosis of infective endocarditis. Of these 66, there were 39 men and 27 women. In 4 of the 66 patients the diagnosis of IE was made from clinical features consistent with the disease but their blood cultures were consistently negative (6.1 percent of total). Of the 66 patients, 44 were intravenous drug abusers (66.6 percent). Seven patients (10.6 percent) had anaerobic or

TABLE 1.—Blood Culture Isolates From 62 Patients With Infective Endocarditis at Rancho Los Amigos Hospital, January 1977 to June 1980

Microorganisms Isolated	Patient Classification	
	Drug Abuser	Non-drug Abuser
Aerobes		
<i>Staphylococcus aureus</i>	27	3
Viridans <i>Streptococcus</i> (α -hemolytic) ..	9	8
Group A <i>Streptococcus</i>	2	1
<i>Pseudomonas aeruginosa</i>	1	0
<i>Enterobacter</i> sp	1	0
<i>Hemophilus aphrophilus</i>	1	0
<i>Streptococcus pneumoniae</i>	0	1
<i>Pasteurella multocida</i>	0	1
<i>Escherichia coli</i>	0	1
<i>Staphylococcus epidermidis</i>	0	1
<i>Eikenella corrodens</i>	1	0
<i>Candida albicans</i>	0	1
TOTAL	42	17
Anaerobic or Microaerophilic Organisms		
Microaerophilic <i>Streptococcus</i>	2	2
<i>Peptostreptococcus</i>	0	1
<i>Bacteroides melaninogenicus</i>	1	0
"Anaerobic <i>Eikenella corrodens</i> "	1	0
<i>Bacteroides</i> sp	1	0
<i>Fusobacterium nucleatum</i>	1	0
<i>Fusobacterium</i> sp	1	0
TOTAL	7	3

microaerophilic endocarditis. Table 1 shows the microorganisms isolated from blood cultures in the 62 patients with positive cultures. Of the ten anaerobic and microaerophilic isolates, seven organisms were isolated from four drug abusers and three were isolated from three who did not use drugs. All seven patients with anaerobic or microaerophilic IE showed features of at least "probable" endocarditis.³ Anaerobes and microaerophiles composed 14.3 percent of the total number of isolates from drug abusers and 15.0 percent of the total number of isolates from non-drug-abusers. It should also be noted that all five of the anaerobic Gram-negative bacilli were isolated from three intravenous drug abusers and that none of the cultures from the nonaddicted patients yielded these organisms. One of the anaerobic Gram-negative bacilli isolated was reported to be an "anaerobic *Eikenella corrodens*," which would not grow aerobically or in 5 percent carbon dioxide (CO₂). The exact biochemical profile of this organism could not be elucidated, but there is a possibility that it could have been *Bacteroides corrodens*.

Table 2 summarizes the clinical features of our seven patients with anaerobic or microaerophilic

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TABLE 2.—Clinical Characteristics of 7 Patients With Anaerobic and Microaerophilic Endocarditis at Rancho Los Amigos Hospital, January 1977 to June 1980

Patient No.	Age	Sex	Intravenous (IV) Drug Abuse (Duration)	Valve(s) Involved	Echocardiogram Positive*	Cardiac Murrur	Probable Source of Infection	Complications	Blood Culture Isolates	Antibiotic Therapy	Outcome
1	22	♀	Methylphenidate hydrochloride, heroin, barbiturates (5 yrs)	Tricuspid	Yes	Yes	IV drug abuse	Septic pulmonary embolism with cavitation	<i>Staphylococcus aureus</i> , microaerophilic <i>Streptococcus</i> , <i>Enterobacter cloacae</i>	Methicillin sodium given IV + gentamicin sulfate + penicillin X 10 wks	Tricuspid valvulotomy. Discharged asymptomatic
2	50	♀	None	Mitral (RHD)	No	Yes	?	Cerebral embolus	<i>Peptostreptococcus</i> sp	Penicillin G given IV X 5 wks; SM given IM X 1 wk	Discharged asymptomatic
3	38	♀	Heroin ("many years")	Porcine tricuspid valve	No	Yes	IV drug abuse	Multiple septic pulmonary emboli; post-operative mediastinitis. Septic shock with gangrene of all extremities requiring amputation	Microaerophilic <i>Streptococcus</i> , <i>Bacteroides melaninogenicus</i>	Penicillin G given IV X 6 wks, gentamicin given IV X 2 wks	Prosthetic tricuspid valvulotomy; after 1 year, amputation of all four extremities; doing well
4	63	♀	None	Starr-Edwards prosthetic mitral valve (RHD)	No	Yes	?	None	Microaerophilic <i>Streptococcus</i>	Vancomycin hydrochloride given IV X 6 wks	Discharged asymptomatic, doing well 6 mos later
5	20	♀	None	Aortic	No	Yes	Multiple dental caries	None	Microaerophilic <i>Streptococcus</i>	Penicillin G given IV X 3 wks; gentamicin given IV X 5 days; penicillin V potassium (Pen-Vee K) by mouth X 2 wks	Discharged asymptomatic

TABLE 2.—Clinical Characteristics of 7 Patients With Anaerobic and Microaerophilic Endocarditis at Rancho Los Amigos Hospital, January 1977 to June 1980 (Continued)

Patient No.	Age	Sex	Intravenous (IV) Drug Abuse (Duration)	Valve(s) Involved	Echocardiogram Positive*	Cardiac Murmur	Probable Source of Infection	Complications	Blood Culture Isolates	Antibiotic Therapy	Outcome
6	37	♀	Methylphenidate (1 yr)	Tricuspid & aortic	Yes	Yes	IV drug abuse, genito-urinary tract after vaginal delivery	Septic pulmonary emboli (recurrence of recent endocarditis)	<i>Bacteroides</i> sp, <i>Fusobacterium nucleatum</i> , <i>Fusobacterium</i> sp	Penicillin G given IV × 6 wks; clindamycin phosphate given IV × 6 wks	Discharged asymptomatic
7	28	♂	Heroin (44 days)	Tricuspid	No	Yes	IV drug abuse	Septic pulmonary emboli with cavitation	"Anaerobic <i>Eikenella corrodens</i> "	Penicillin G given IV × 6 wks	Discharged asymptomatic

IM = intramuscularly; IV = intravenously; RHD = rheumatic heart disease; SM = streptomycin sulfate.

* = Either valvular thickening, vegetations, or both.

infective endocarditis. The patients' ages ranged from 20 to 63, with the ages of the four drug abusers ranging from 22 to 38 (mean = 31.2) and that of the three nonabusers from 20 to 63 (mean = 44.3). Six of our seven patients were women. Two patients (Nos. 2 and 4) had a previous history of rheumatic heart disease (RHD) and one of these had a Starr-Edwards mitral valve prosthesis. Patient No. 3 had a recently treated endocarditis, which suggested a reinfection with other microorganisms after an uncomplicated vaginal delivery. All in all, three of the seven cases (43 percent) had preexistent valvular damage, with two patients having prosthetic valves in place. The tricuspid valve was infected in all four drug abusers, one of whom had a porcine tricuspid valve. One of these four patients had simultaneous involvement of the aortic valve. Two of the three nonabusers had involvement of the mitral valve (one of them had the Starr-Edwards mitral valve prosthesis) and the third had aortic valve involvement. The mouth was considered to be the source of infection in one patient (a nonabuser with multiple carious teeth) and another (a drug abuser) was presumed to have acquired the infection following vaginal delivery. All of the drug abusers had radiologic and clinical evidence of septic pulmonary embolism to the lungs, in two cases progressing to frank cavitation.

All three nonabusers had a single-organism IE with either an anaerobic or microaerophilic *Streptococcus*. Three of the four drug abusers exhibited polymicrobial IE; in each of these three patients blood cultures yielded three microorganisms simultaneously. One patient had purely anaerobic endocarditis, a second had one aerobe plus one microaerophile plus one anaerobe and the third patient had two aerobes plus one microaerophile.

Two patients (both drug abusers) required tricuspid valvectomy, for persistent fever and generally poor clinical response to antibiotic therapy. Patient No. 1 had sterile blood cultures before valvectomy, which was done five weeks after antibiotic therapy was initiated. Cultures of the excised affected valve were sterile, but the patient's fever subsided after the surgical procedure while on the same antibiotic regimen. Another patient (No. 3) had a porcine tricuspid valve excised a week after antibiotic drugs were started when she had persistent fever, positive blood cultures and continued evidence of pulmonary embolism. Culture of the excised valve was

positive, and she had a stormy postoperative course characterized by mediastinitis (requiring tube drainage) and septic shock followed by gangrene necessitating amputation of all four extremities. She survived all these complications and repeat blood cultures continued to be sterile until discharge.

One patient (No. 4) with a microaerophilic streptococcal endocarditis involving a Starr-Edwards mitral valve prosthesis responded to a six weeks' course of antimicrobial therapy without need for prosthetic valve replacement. The remaining patients responded to courses of parenteral administration of antibiotic therapy ranging from five to ten weeks.

Comment

The 10.6 percent incidence of infective endocarditis due to anaerobic or microaerophilic microorganisms appears to be higher than the previously recorded incidence in the literature.¹ The high proportion of intravenous drug abusers in our patient population (66.6 percent) invited speculation of a possible relationship between the two observed events. However, a review of the literature on endocarditis in those who practiced intravenous drug abuse revealed a very low incidence of anaerobic or microaerophilic endocarditis (0 percent to 6 percent) in this patient population.⁷⁻¹¹ In addition, the incidence of anaerobic and microaerophilic IE was very comparable in our drug-abuser and non-drug-abuser populations. One interesting observation, however, was the confinement of anaerobic Gram-negative bacillary endocarditis to the drug-abuser group (patients No. 3, 6 and 7). Nastro and Finegold¹² reviewed the literature on anaerobic Gram-negative bacillary endocarditis and found only one drug abuser in 37 patients. It is possible that blood culture techniques more conducive to the isolation of anaerobic and microaerophilic microorganisms accounted for this relatively high incidence of anaerobic and microaerophilic IE in our patient population. Our low (6.1 percent) incidence of blood-culture-negative IE may also indicate a better recognition of these cases that would have otherwise been missed. The incidence of IE with negative blood cultures in the literature has generally ranged from 13 percent to 23 percent.¹³ The relatively large amount of blood (10 ml) inoculated in 90 ml of broth culture medium theoretically could have facilitated the isolation of micro-

organisms from patients who may not consistently have at least one microorganism per milliliter of blood.

That all five of the patients (of the 66 cases at Rancho Los Amigos Hospital) with polymicrobial endocarditis were drug abusers was not surprising. Previous reviews have reported a varying incidence (2 percent to 9 percent) of polymicrobial endocarditis in drug addicts.⁷⁻¹⁰ A review of polymicrobial bacteremia¹⁴ also showed that three of 88 patients reviewed practiced intravenous drug abuse. These three patients were the only ones with endocarditis in that series.

An unexpected finding in our series was the fact that six of the seven patients (86 percent) in this series with anaerobic or microaerophilic endocarditis were women, although only 41 percent of the total IE population were. Analysis using the Fischer's exact test, however, revealed that the difference was not statistically significant ($P = .06$). In Nastro and Finegold's¹² review of anaerobic Gram-negative bacillary IE 65 percent of their population were men. In only one of our patients (No. 6) was the genitourinary tract a probable source of IE (that is, endocarditis occurred after a normal vaginal delivery).

One of our seven patients (No. 2) suffered from cerebral embolism. All four of our drug abusers had involvement of the tricuspid valve with concomitant septic pulmonary embolism. The incidence of serious systemic embolism originating from the left side of the heart in our patients is lower than the 60 percent incidence in Felner and Dowell's series.¹

All seven of our patients survived their infection. Two patients required tricuspid valvectomy to control it. In one of these patients (No. 3) mediastinitis developed, along with septic shock and gangrene of all four extremities requiring amputation; she nevertheless survived. Our 0 percent mortality is considerably better than the 21 percent to 46 percent mortality previously reported for IE due to anaerobic or microaerophilic bacteria.^{1,12} The good response to antibiotic therapy in our patients is exemplified by patient No. 4, who was cured of prosthetic mitral valve endocarditis without resort to valve replacement. It should be pointed out, however, that none of our patients had *Bacteroides fragilis* endocarditis. This organism is frequently resistant to penicillin and may have contributed to the higher mortality in previous reports. In our limited experience, however, an-

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aerobic and microaerophilic infective endocarditis due to organisms other than *B fragilis* may not necessarily imply a bleak prognosis.

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ARTICLES TO READ IN OTHER JOURNALS

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The Placenta: How to Examine It and What You Can Learn

Benirschke K

Contemporary OB/GYN

1981 Mar; 17:117-126

DISCIPLINES: Obstetrics, Family Practice, Pediatrics

READABILITY: Excellent

The author, known throughout the medical world for his knowledge of the placenta, warns us not to simply drop that organ into the bucket. He reminds us that a step-by-step examination of the placenta can give us retrospective information on the intrauterine life as well as predictions as to the future life of the infant.

—E. R. W. FOX, MD
Coeur d'Alene, ID

Rubella Outbreak Among Hospital Employees

Strassburg MS, Imagawa DT, Fannin SL, et al

Obstetrics & Gynecology

1981 Mar; 57:283-288

DISCIPLINES: All Physicians (especially Hospital Administrators, House Staff, Public Health)

READABILITY: Very good

Today many young adults are rubella susceptible. Because of immunization of children, these people have never been exposed to wild virus infection. Outbreaks of rubella infections have occurred in this age group. The authors present excellent guidelines for testing and immunizing health workers who might expose women in early pregnancy.

—E. R. W. FOX, MD
Coeur d'Alene, ID