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Experimental *Eikenella corrodens* Endocarditis in Rabbits

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The ability of *Eikenella corrodens* to cause endocarditis in catheterized rabbits was studied. *E. corrodens* 1073, the serum-resistant strain used in the study, was isolated from a human periodontitis lesion. Thirty-four rabbits, surgically catheterized across the aortic valve and injected intravenously 24 to 48 h later with 10^7 to 10^9 log-phase organisms, were studied. Only three rabbits developed positive blood cultures and only two rabbits died before the time of sacrifice at 14 days after infection. Autopsies showed that all rabbits developed aortic vegetations, 52% of which were culture positive for *E. corrodens*. The organisms were recovered from aortic vegetations in a mean concentration of $10^{5.3}$ colony-forming units/g of tissue and from liver or kidney in 28% of the animals in concentrations from 10^2 to 10^4 colony-forming units/g. Indirect immunofluorescent staining of vegetations, with the use of specific rat antiserum to *E. corrodens* 1073 and fluorescein isothiocyanate-labeled goat antirat serum, revealed colonies of *E. corrodens* in culture-negative vegetations as well as in those which were culture positive. The results showed that *E. corrodens* was an effective pathogen in the rabbit model of endocarditis, in which the disease was infrequently bacteremic and rarely fatal.

Eikenella corrodens is a gram-negative, asaccharolytic, facultative anaerobe indigenous to the human oral cavity. Since its initial description (8, 11) and later classification by Jackson (12, 13), this organism has been recovered as the sole isolate and in mixed flora from numerous infections (2, 5), including three documented cases of endocarditis (10, 25). We have isolated *E. corrodens* from 40% of healthy mouths as a minor constituent of the autochthonous gingival flora (S. J. Badger and J. Peterson, submitted for publication). Socransky (24) has shown this organism to be a predominant isolate from deep gingival pockets of some patients with periodontal disease, and Khairat (16) recovered *E. corrodens* from blood in 16 of 64 patients 1 min after tooth extraction.

The need for a better understanding of *E. corrodens* as a pathogen for endocarditis arises from the high prevalence of periodontal disease in the population (20), the possibility of high concentrations of *E. corrodens* in periodontal pockets as a source of bacteremia, and the potential hazard of bacteremia to persons with prosthetic valves or damaged endocardium. The aim of the following study was to investigate the ability of *E. corrodens* to colonize damaged heart valves and cause disease in rabbits.

In the rabbit model of endocarditis described by Garrison and Freedman (9) and modified by Durack et al. (6), human endocarditis pathogens produce fatal disease accompanied by fever, bacteremia, infected vegetations, and metastatic infection. Using this model, we found that *E. corrodens* produces endocarditis in rabbits that is seldom fatal or bacteremic. Our results suggest that this pathogen, in contrast to other endocarditis pathogens, may cause mild and self-limited infections.

MATERIALS AND METHODS

Bacterial strains. *E. corrodens* 1073, used in this study, was isolated by Newman et al. (19) from the deep gingival pocket of a patient with periodontitis. The strain was extensively characterized by A. C. R. Crawford et al. (J. Dent. Res., Abstr. no. 1005, 1976) and was found to cause extensive alveolar bone resorption in mono-infected rats (18). *E. corrodens* 1073 is the same strain which Johnson et al. (14) designated CS10B. *E. corrodens, Bacteroides corrodens*, and two strains of *Actinobacillus actinomycetem-comitans* were supplied by S. S. Socransky. *Haemophilus* strains supplied by T. Gavin included: *H. influenzae* CDC 76-0884 and CDC 79-84403, and Cleveland Clinic isolates of *H. parainfluenzae, H. parahaemolyticus,* and *H. aphrophilus* (two strains). C. W. Shuster supplied the strain of *Escherichia coli* K-12 C600. *Cardiobacterium hominis* was an oral isolate from this laboratory.

Serum sensitivity of *E. corrodens* 1073. Strain 1073 was tested for sensitivity to normal rabbit serum and complement by the method described by Durack and Beeson (7). Sera from four rabbits were pooled after the individual sera were shown to be free from anti-*E. corrodens* agglutinins. Samples containing 10^3 organisms from an 18-h CS3 broth (see below) culture were incubated in: (i) autoclaved CS3 broth plus 10% fresh rabbit serum, (ii) CS3 broth plus 10% heated rabbit serum, and (iii) CS3 broth alone. Duplicate 0.1-ml samples were plated for enumeration at zero time, 1 h, and 2 h. *E. coli* K-12 C600, a serum-sensitive organism, was tested by the same procedure in Hanks balanced salt solution (HBSS). *E. corrodens* was studied in CS3 broth rather than HBSS because it did not remain viable in HBSS during the period of incubation.

Culture methods. For inoculation of rabbits, *E. corrodens* was grown in broth (CS3) containing the following ingredients per liter of distilled water: Trypticase (BBL), 17.0 g; Phytone (BBL), 3.0 g; potassium nitrate, 1.0 g; sodium formate, 1.0 g; and hemin, 3 mg. Hemin was added as 1 ml of a 0.3% sterile solution in 1 M sodium carbonate. Incubation of all cultures was at 37°C under an atmosphere of 80% Ar, 10% CO_2, and 10% H_2, in a gas-replacement jar containing Pd catalyst. After 18 h of incubation, cultures were centrifuged, washed in phosphate-buffered saline, pH 7.2 (PBS), and resuspended to an optical density at 540 nm of 0.82, or 10^9 cells/ml. Viability was checked by serial dilution plate counts on Trypticase soy agar containing 5% sheep blood (SBA).

Rabbit blood for culture was drawn into a heparinized syringe from the central ear artery or marginal vein. A 1-ml amount was cultured in 10 ml of CS3 broth, and 0.1 ml was streaked on SBA. After 3 days, all broth cultures were streaked on SBA to check for the growth of corroding colonies which are typical of *E. corrodens*. Blood agar plates were incubated for 6 days before being read.

Organisms in homogenized tissue specimens were enumerated by making four 10-fold serial dilutions of homogenates in CS3 broth. Amounts of 0.1 ml of the original homogenate and the 10^{-1} dilution were streaked on SBA. All tubes showing growth after 3 days of incubation were streaked on SBA for observation of colony morphology, and typical colonies were tested by slide agglutination with specific rabbit antiserum to confirm the presence of *E. corrodens*.

Production of *E. corrodens* endocarditis. Polyethylene catheters (18.5-gauge Intracath; C. R. Bard Co., Inc., Murray Hill, N.J.) were surgically implanted (by the technique of Garrison and Freedman [9]) in 34 New Zealand white rabbits weighing 2 to 3 kg. Anesthesia was given as intramuscular injections of ketamine hydrochloride (Ketaset; Bristol Laboratories, Syracuse, N.Y.), 35 mg/kg, and xylazine (Rompun; Chemagro, Kansas City, Mo.), 5 mg/kg. The right carotid artery was exposed, ligated, and catheterized across the aortic valve. The catheter end was tied and the skin was sutured over the catheter, which was left in situ for the duration of the experiment. At 1 to 2 days after surgery, the animals were injected intravenously with approximately 10^9 washed cells of *E. corrodens* 1073 determined by optical-density measurement of cultures. Every 2 days, the animals were weighed, their temperatures were taken, and heparinized blood specimens were obtained for culture. At the end of 1 to 3 weeks, the rabbits were sacrificed by intraperitoneal injection of pentobarbital. Aortic valve vegetations and specimens of liver, spleen, and kidney were aseptically removed, weighed, homogenized, and cultured.

Serological studies. Serum was collected from all rabbits prior to surgery and prior to autopsy. The microagglutination test for serum titer was done in microtiter plates with 0.025-ml diluters (Cooke Engineering Co., Alexandria, Va.). Washed cells of a 24-h CS3 broth culture were adjusted to a McFarland no. 9 standard with PBS and were used as antigen. Unheated test sera were diluted with PBS through 12 serial twofold dilutions. Control wells contained presurgery serum from the same rabbit as the test sample. One drop (0.025 ml) of cell suspension was added to each well. The plates were shaken for 10 min at room temperature, incubated for 20 min at 37°C, and read under a dissecting microscope with reflected light. The titer was recorded as the reciprocal of the highest dilution showing agglutination. Duplicate determinations were within one dilution of each other.

Pathological studies. Sections of vegetations, cardiac muscle, liver, spleen, and kidney were taken at autopsy, fixed in 10% buffered Formalin, and sectioned for histological staining with hemotoxylin and eosin and Gram stains.

Indirect immunofluorescence in tissues. Samples of each tissue for indirect fluorescent staining were embedded in O.C.T. compound (Lab Tek Products, Naperville, Ill.) in tissue carrier mounts (TIMS; Lab-Line Biomedical Products, Melrose Park, Ill.) and then immersed in liquid N_2 and stored in a Revco freezer at −80°C until sectioned. Frozen tissue blocks were sectioned 6 μm thick in a cryostat and air-dried on slides. Visualization of *E. corrodens* in frozen tissue sections was accomplished as follows: application of specific rat anti-*E. corrodens* 1073S serum, thorough washing in PBS, application of fluorescein isothiocyanate (FITC)-conjugated immunoglobulin G fraction of goat antirat serum, and a final washing in PBS. Specific rat serum was prepared in outbred albino Sprague-Dawley rats (average weight, 210 g) by four weekly injections of live *E. corrodens* 1073S. Each animal was given 10^9 organisms intravenously in 0.5 ml of PBS and 10^9 cells subcutaneously in 0.5 ml of incomplete Freund adjuvant per injection. Sera of like titer were pooled. The highest agglutination titer was 1,280, and this was used at a dilution of 1:10. The FITC-goat antirat serum (Cappel Laboratories, Inc., Downington, Pa.) had a fluorescein to protein ratio of 3.5 and was diluted 1:10 with PBS before use.

The stained slides were mounted in a drop of fluorescent-antibody mounting fluid, pH 9 (Difco Laboratories, Detroit, Mich.), sealed under cover slips, and examined in a Leitz Wetzlar Ortholux microscope equipped with a fluorescence vertical illuminator and an automatic Leicaflex camera system.

The specific rat serum showed no cross-reaction by indirect immunofluorescence when used to stain the following organisms: *A. actinomycetem-comitans* 511,

B. corrodens 1084, *H. influenzae* (two strains), *H. parainfluenzae*, *H. parahaemolyticus*, and *H. aphrophilus* (two strains). *H. influenzae* CDC79-84403 and *A. actinomycetem-comitans* 2043 showed 1+ fluorescence at a serum dilution of 1:10 and no staining at a dilution of 1:20.

RESULTS

Serum sensitivity of *E. corrodens* 1073. Figure 1 shows that *E. corrodens* 1073 is resistant to the bactericidal action of normal rabbit serum. The plotted values for surviving organisms are the mean of three determinations. Complement activity of the pooled serum was demonstrated by the rapid killing of *E. coli* K-12 C600.

Clinical features of infection. Thirty-four rabbits with catheters and five noncatheterized controls were inoculated with *E. corrodens*. Five rabbits died within 24 h after inoculation; their deaths were attributed to acute toxicity produced by the inoculated bacteria, and they were not included in the following observations. Of the rabbits which survived longer than 48 h after injection, 52% (15 rabbits) had aortic vegetations from which *E. corrodens* colonies were cultured (Table 1) and were thus considered to have endocarditis at the time of autopsy. Two rabbits died of the infection after the 48-h period, on days 4 and 8; the remainder were sacrificed at a mean time of 14 days after injection.

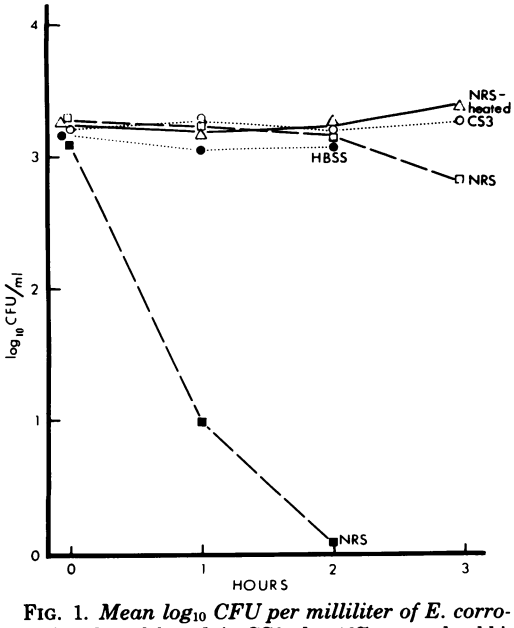

FIG. 1. *Mean $\log_{10}$ CFU per milliliter of E. corrodens incubated for 3 h in CS3 plus 10% normal rabbit serum (NRS)* (□), *CS3* (○), *or CS3 plus heated NRS* (△) *and of E. coli K-12 C600 incubated in HBSS* (●) *and in HBSS plus 10% NRS* (□).

Temperature readings, with above 39.6°C denoting fever, rose rapidly to a peak mean of 41.4°C between 2 and 3 h postinjection and returned to normal within 48 h. Catheterized rabbits and five noncatheterized control animals showed no difference in this early fever response to injected organisms. Among catheterized animals 60% of the recorded temperatures subsequent to 48 h were in the febrile range. Control animals showed only occasional mild fever (Table 1).

Weight loss occurred in 28 of the 29 infected rabbits. The mean loss was 0.23 kg, with a range of 0.02 to 0.73 kg. The lowest weights occurred at a mean time of 6 days after inoculation, and 40% of the animals had regained their weights by the time of autopsy. Control animals (inoculated but not catheterized) showed a mean weight gain of 0.24 kg in 14 days.

For estimation of the clearance of *E. corrodens* from the circulation, blood specimens were taken at intervals of 5 min, 5 h, and 24 h after injection of 10^9 organisms. Bacterial clearance was complete by 24 h in 28 of 29 rabbits. Samples taken 5 min after injection yielded a mean concentration of $10^{5.3}$ colony-forming units (CFU)/ml of blood, and less than 10 CFU/ ml of blood remained at 5 h. Table 1 shows that bacteremia was rare (8 of 174 cultures were positive) after the initial clearance. The positive cultures were from only three rabbits.

Bacteriological findings. At autopsy, all 29 animals were seen to have developed vegetations on or surrounding the aortic valves. Some of the vegetations had extended to the aortic wall, and frequently the catheter tip was buried in a vegetation. Aortic vegetations from 15 animals were culture positive, yielding *E. corrodens* in numbers ranging from $10^{2.2}$ to $10^{5.8}$, with a mean of $10^{5.3}$ CFU/g of tissue. Weights of vegetations varied from 2 to 100 mg. Small numbers (10^2 to 10^4 CFU/g of tissue) of *E. corrodens* were recovered from kidney sections from 5 of the 29 rabbits and from liver sections from 3 of the 29 rabbits. Two rabbits which had positive liver cultures showed no growth from culture of aortic vegetations. The two animals that died during the course of the experiment had positive liver cultures although only one of them yielded *E. corrodens* from the aortic vegetation.

Agglutinating antibody response. The presurgery specific anti-*Eikenella* agglutinin titer of all rabbits was zero. Blood specimens taken at time of autopsy had measurable agglutination titers ranging from 16 to 256. There was no correlation between culture-positive vegetations and agglutinating titer, since the geometric mean titer of culture-positive rabbits was 33 and

TABLE 1. *Features of experimental Eikenella corrodens infection*

Group	No. of rabbits	No. of deaths	Mean wt change (kg)	No. of elevated temperature readings[a]/total		No. of positive cultures		Geometric mean of agglutination titer[c]
				≥39.7°C	≥40.0°C	Blood[b]	Liver or kidney	
Catheterized with culture-positive vegetations at autopsy	15	1	−0.24	49/83	19/83	6 (1)	3	33
Catheterized with culture-negative vegetations at autopsy	14	1	−0.12	41/91	12/91	2 (2)	5	59
Noncatheterized controls infected with *E. corrodens*	5	0	+0.24	10/30	0	0	0	42

[a] Later than 48 h after infection.
[b] Figures in parentheses show the number of animals.
[c] At 14 days after infection.

that of culture-negative rabbits was 59 ($t = 1.278$, Student's t test). Noncatheterized, infected control animals showed a similar mean titer (42) at 2 weeks.

Pathological studies. Histological examination of vegetations, kidneys, spleen, and liver were performed in 26 of the rabbits studied. We could obtain sufficient amounts of tissue for histological examination from only 18 vegetations. These vegetations consisted of 12 from the aortic valve and 6 from the ventricular wall. The histological composition of these vegetations showed that 7 of them had early inflammatory responses, 8 had early organizing inflammatory responses, and 3 had mixed early and organizing vegetations. Early vegetations were characterized by fibrin deposits with platelet aggregates, necrotic debris, and polymorphonuclear leukocytes. Early organizing vegetations were characterized by proliferating fibroblasts and endocardial cells, fibrous tissue, and a few macrophages. Dystrophic calcifications were present in 1 of the 8 early organizing (Fig. 2) and 2 of the 3 mixed vegetations. *E. corrodens* was cultured from 4 of the 7 early, 3 of the early organizing, and all of the mixed vegetations.

Examination of the kidneys of 26 rabbits revealed that 18 had normal morphology and 8 had cortical infarcts. The cortical infarcts were triangular in shape and well demarcated, having their bases on the cortical surface and their apices at the medulla. Seven of the infarcts were ischemic in nature without inflammatory cell infiltration, and one infarct revealed an acute inflammatory cell infiltrate. One of the infarcts had dystrophic calcification. These features were consistent with infarction due to arterial occlusion by emboli from cardiac vegetations. *E. corrodens* was cultured from 2 of 8 infarcts and 3 of 18 normal kidneys.

Spleens of 26 rabbits revealed follicular reactive hyperplasia in 14 animals and either normal morphology or acute congestion in 12. Reactive hyperplasia was characterized by increased numbers and size of lymphoid follicles with prominent germinal centers and increased numbers of inflammatory cells in the sinusoids. Cultures of splenic tissue were positive in only one case.

Histology of livers showed entirely normal tissue in 24 rabbits and occasional granulomas in 2. Cultures of liver grew *E. corrodens* in only 3 cases.

Indirect immunofluorescent staining. Gram-negative organisms could not be demonstrated in tissue sections by a Gram stain procedure. Frozen tissue sections of valvular vegetations from three culture-positive rabbits and from three culture-negative rabbits were stained by indirect immunofluorescence. *E. corrodens* colonies (Fig. 3) were observed in all vegetations, and the numbers of colonies were similar in those which had not yielded viable bacteria and those from which organisms grew.

DISCUSSION

E. corrodens produced endocarditis in catheterized rabbits that was clinically mild, rarely fatal, and seldom bacteremic, and resulted in positive cultures of endocardial vegetations in about half of the infected rabbits. This experimental infection contrasts sharply with endocarditis in catheterized rabbits caused by the classical pathogens viridans streptococci, *Streptococcus faecalis*, and *Staphylococcus aureus*, which are fatal within 2 weeks and produce continuous bacteremia (22, 23). *E. corrodens* endocarditis more nearly resembles experimental endocarditis caused by the gram-negative pathogens *Neisseria gonorrhoeae* (15) and *Pseudomonas*

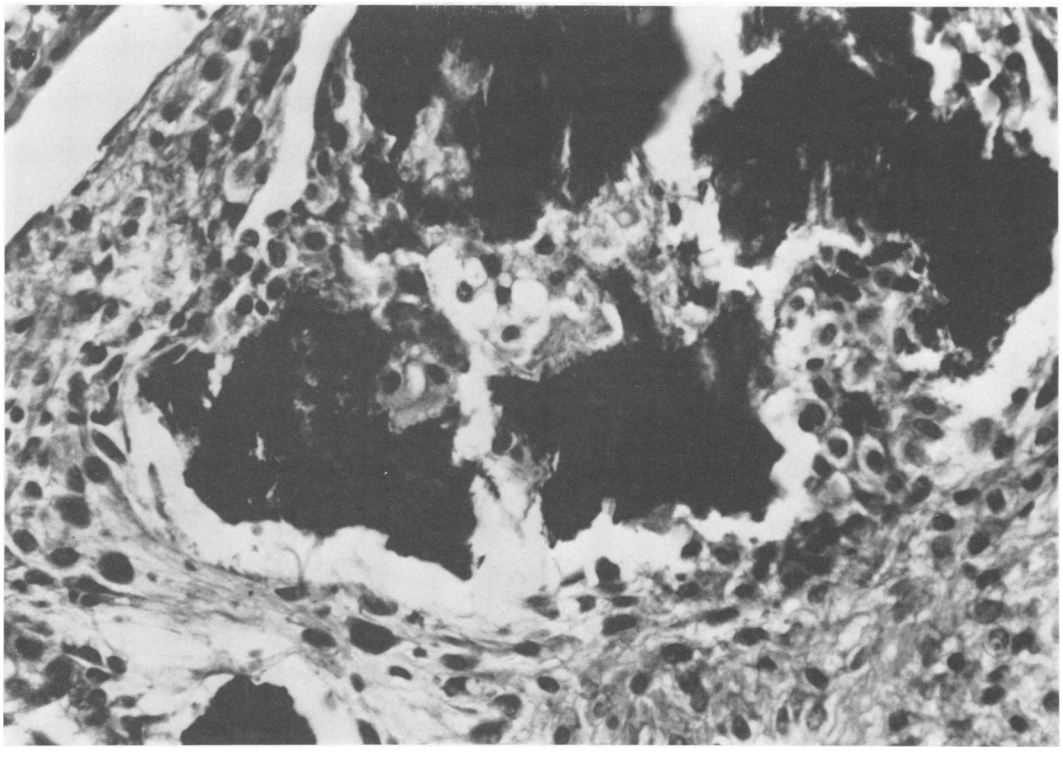

FIG. 2. *Section of a culture-negative aortic vegetation from a rabbit with E. corrodens endocarditis stained with hematoxylin and eosin. Dystrophic calcium deposits are surrounded by proliferating fibroblasts. A few macrophages but no acute inflammatory cells are seen.* × *500.*

aeruginosa (1), which were less commonly fatal (33 to 78%) and infrequently or intermittently bacteremic.

The results of our studies suggest, nevertheless, that *E. corrodens* is an effective pathogen in this rabbit model. Rabbits were challenged with a high dose of organisms, 10^7 to 10^9 viable bacteria, which was near the lethal dose, as shown by the deaths of several rabbits within 24 h of inoculation. Whether smaller numbers of bacteria, which might approximate the exposure of persons to transient bacteremia during dental procedures, could also produce infection was not tested in this study.

Of 29 infected rabbits, 15 had positive cultures of aortic vegetations which yielded *E. corrodens* at a mean concentration of $10^{5.3}$ CFU/g of tissue. Although the remaining 14 rabbits had negative cultures of vegetations, they had clinical and pathological features similar to those of the rabbits with positive cultures. Furthermore, 5 of the rabbits which yielded no growth from vegetations had positive cultures of liver or kidney at autopsy, suggesting that infected emboli from vegetations had recently been implanted in these organs. Additional evidence for infection in culture-negative vegetations was obtained by applying indirect immunofluorescent staining to tissues. Vegetations from 6 rabbits (3 with positive cultures, 3 with negative cultures) were examined, and all revealed clusters of fluorescent bacilli. These findings suggested that *E. corrodens* was more frequently present in tissues than our culture results indicated. This inability to culture *E. corrodens* from some of the rabbits may have resulted from the fastidious nature of the organism that allowed it to die during the processing of tissues prior to culture or from the organism's being nonviable in tissues during the convalescent stages of infection.

The importance of *E. corrodens* as a human pathogen has been recently reviewed (2). Three cases of endocarditis caused by *E. corrodens* have been reported (10, 25), and one case was fatal. The fastidious nature of this slow-growing organism, which requires CO_2 and hemin for growth, suggests that some cases of *E. corrodens* infection in humans are never recognized. The high frequency of negative blood cultures in our rabbits in the face of infected valves indicated that this infection, like fungal endocarditis caused by *Candida albicans* (21) and *Aspergillus fumigatus* (3), is not often accompanied by bacteremia; thus, the time-honored method of

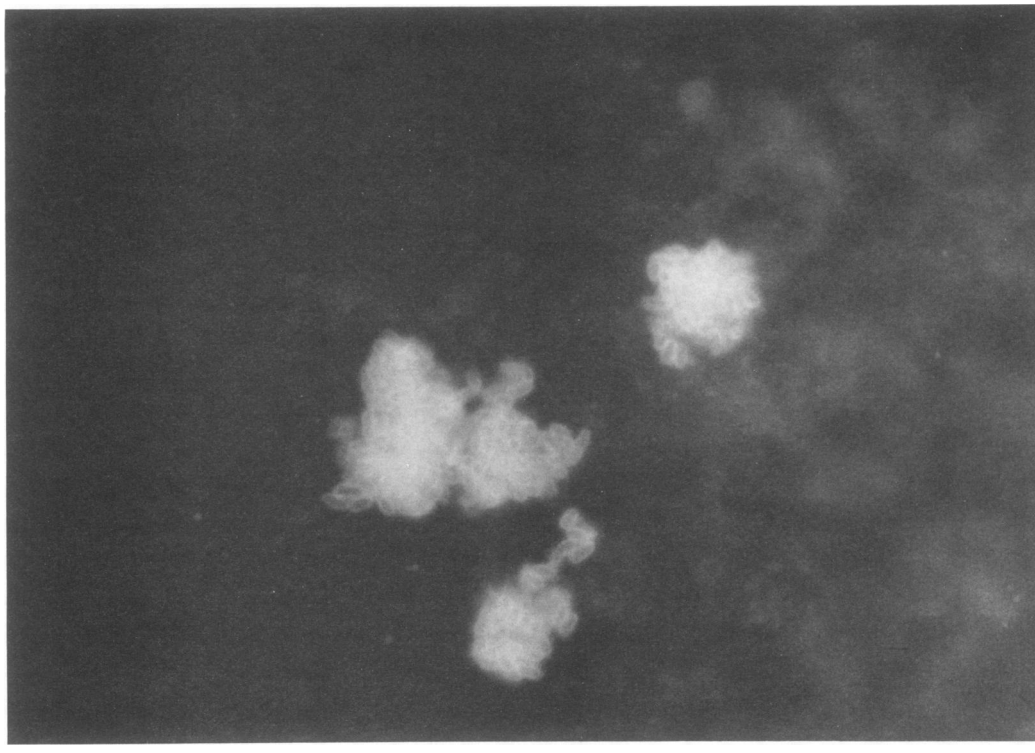

FIG. 3. *Section of the same vegetation as in Fig. 2 showing colonies of Eikenella stained with specific rat anti-Eikenella serum and FITC-goat antirat serum. Duration of infection was 14 days.*

culturing blood may not always be useful in diagnosing endocarditis. In a large series of patients with endocarditis confirmed by autopsy, 30% of them had had negative blood cultures before death (4). Some cases could be caused by fastidious pathogens such as *E. corrodens,* which either infrequently produce bacteremia or cannot be recovered by standard blood culture techniques.

Specific agglutinins to *E. corrodens* appeared in all 29 rabbits during the course of infection. Our study suggests that an alternative method of identifying the etiological agent of endocarditis may include determination of specific agglutinating antibody titers. Immunofluorescent staining of valvular tissues might allow retrospective diagnosis of culture-negative endocarditis.

Our study further suggests that *E. corrodens,* by producing clinically mild and nonfatal infections, may be a cause of self-limited endocarditis. There is a rising incidence of elderly patients with degenerative and calcific valvular heart disease of unknown etiology. The lesions of periodontal disease are a constant source of bacteremia due to opportunistic fastidious oral organisms. These organisms gain easy access to the blood stream during dental manipulations (16). Repeated, subclinical episodes of self-limited endocarditis could produce chronic valvular damage. Some of our rabbits showed calcified vegetations, and most had fibroblasts and chronic inflammatory cells in a process that was subacute or resolving. Further studies with this model will be required to examine immunological mechanisms of recovery and the later effects of infection on endocardial tissue.

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LITERATURE CITED

1. **Archer, G., and F. R. Fekety, Jr.** 1977. Experimental endocarditis due to *Pseudomonas aeruginosa*. II. Therapy with carbenicillin and gentamicin. J. Infect. Dis. **136**:327-335.
2. **Brooks, G. F., J. M. O'Donoghue, and J. P. Rissing.** 1974. *Eikenella corrodens,* a recently recognized pathogen: infections in medical-surgical patients and in association with methylphenidate abuse. Medicine **53:** 325-342.
3. **Carrizosa, J., C. Kohn, and M. E. Levison.** 1975. Experimental aspergillus endocarditis in rabbits. J. Lab.

Clin. Med. **86**:746–753.
4. **Cherubin, C. E., and H. C. Ness.** 1971. Infective endocarditis at the Presbyterian Hospital in New York City from 1938–1967. Am. J. Med. **51**:83–96.
5. **Dorff, G. F., L. J. Jackson, and M. W. Rytel.** 1974. Infections with *Eikenella corrodens*, a newly recognized human pathogen. Ann. Intern. Med. **80**:305–309.
6. **Durack, D. T., and P. B. Beeson.** 1972. Experimental bacterial endocarditis. I. Colonization of sterile vegetation. Br. J. Exp. Pathol. **53**:44–53.
7. **Durack, D. T., and P. B. Beeson.** 1977. Protective role of complement in experimental *Escherichia coli* endocarditis. Infect. Immun. **16**:213–217.
8. **Eiken, M.** 1958. Studies on anaerobic, rod-shaped, gram-negative micro-organism: *Bacteroides corrodens* n. sp. Acta Pathol. Microbiol. Scand. **43**:404–416.
9. **Garrison, P. K., and L. R. Freedman.** 1970. Experimental endocarditis. I. Staphylococcal endocarditis in rabbits resulting from placement of a polyethylene catheter in the right side of the heart. Yale J. Biol. Med. **42**: 394–410.
10. **Geraci, J. E., P. E. Hermans, and J. A. Washington II.** 1974. *Eikenella corrodens* endocarditis. Mayo Clin. Proc. **49**:950–953.
11. **Henriksen, S. D.** 1948. Studies on gram-negative anaerobes. II. Gram-negative anaerobic rods with spreading colonies. Acta Pathol. Microbiol. Scand. **25**:368.
12. **Jackson, F. L., and Y. E. Goodman.** 1972. Transfer of the facultatively anaerobic organism *Bacteroides corrodens* Eiken to a new genus, *Eikenella*. Int. J. Syst. Bacteriol. **22**:73–77.
13. **Jackson, F. L., Y. E. Goodman, F. R. Bel, P. C. Wong, and R. L. S. Whitehouse.** 1971. Taxonomic status of facultative and strictly anaerobic "corroding bacilli" that have been classified as *Bacteroides corrodens*. J. Med. Microbiol. **4**:171–184.
14. **Johnson, D. A., U. H. Behling, C. H. Lain, M. Listgarten, S. Socransky, and A. Nowotny.** 1978. Role of bacterial products in periodontitis: immune response in gnotobiotic rats monoinfected with *Eikenella corrodens*. Infect. Immun. **19**:246–253.
15. **Kaspar, R. L., and D. J. Drutz.** 1977. Perihepatitis and hepatitis as complications of experimental endocarditis due to *Neisseria gonorrhoeae* in the rabbit. J. Infect. Dis. **136**:37–41.
16. **Khairat, O.** 1967. *Bacteroides corrodens* isolated from bacteremias. J. Pathol. Bacteriol. **94**:29–40.
17. **Labbe, M., W. Hansen, E. Schoutens, and E. Yourassowsky.** 1977. Isolation of *Bacteroides corrodens* and *Eikenella corrodens* from human clinical specimens. Infection **5**:159–162.
18. **Listgarten, M. A., D. Johnson, A. Nowotny, A. C. R. Tanner, and S. S. Socransky.** 1978. Histopathology of periodontal disease in gnotobiotic rats monoinfected with *Eikenella corrodens*. J. Periodontal Res. **13**:134–148.
19. **Newman, M. G., S. S. Socransky, E. D. Savitt, D. A. Propas, and A. Crawford.** 1976. Studies of the microbiology of periodontosis. J. Periodontol. **47**:373.
20. **Nolte, W. A. (ed.).** 1977. Oral microbiology, p. 491. C. V. Mosby Co., St. Louis, Mo.
21. **Sande, M. A., C. R. Bowman, and R. A. Calderone.** 1977. Experimental *Candida albicans* endocarditis: characterization of the disease and response to therapy. Infect. Immun. **17**:140–147.
22. **Sande, M. A., and R. G. Irvin.** 1974. Penicillin-aminoglycoside synergy in experimental *Streptococcus viridans* endocarditis. J. Infect. Dis. **192**:572–576.
23. **Sande, M. A., and M. L. Johnson.** 1975. Antimicrobial therapy of experimental endocarditis caused by *Staphylococcus aureus*. J. Infect. Dis. **131**:367–375.
24. **Socransky, S. S.** 1977. Microbiology of periodontal disease—present status and future considerations. J. Periodontol. **48**:497–504.
25. **Watsky, D.** 1977. Microbiology problem. Am. J. Med. Technol. **43**:781.