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Antimicrobial Susceptibilities of *Erysipelothrix rhusiopathiae*

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The in vitro susceptibilities of 10 isolates of *Erysipelothrix rhusiopathiae* to 16 antimicrobial agents were determined. Penicillin and imipenem were the most active agents, followed by piperacillin, cefotaxime, ciprofloxacin, pefloxacin, and clindamycin. Some resistance was observed with erythromycin, tetracycline, and chloramphenicol. Activity was poor or absent with vancomycin, teicoplanin, daptomycin, trimethoprim-sulfamethoxazole, gentamicin, and netilmicin.

Erysipelothrix rhusiopathiae is a gram-positive bacillus that has long been recognized as pathogenic for animals and humans (2, 9, 15). The clinical spectrum of human infection with this organism varies from a mild, localized, self-limiting cutaneous disease often involving the fingers (erysipeloid) to a systemic infection frequently associated with endocardial infection (1, 2, 14). In a recent review of the literature, Gorby and Peacock (2) found that 49 cases of systemic infection with *E. rhusiopathiae* have been reported over the past 15 years; 90% of these were episodes of proven or presumed endocarditis. Because of this small number of reported cases of systemic human infection with *E. rhusiopathiae*, antibiotic susceptibility data are very limited. Overall, *E. rhusiopathiae* seems to be very susceptible to penicillin and to cephalosporins (2, 9, 12–14); however, alternatives to these antibiotics have been rarely used in therapy, and the MICs and MBCs of many other antibiotics for this organism are not widely known (9). In view of the above, it seemed appropriate to evaluate the antimicrobial susceptibility of *E. rhusiopathiae* to old and new antibiotics that are currently suggested or potentially useful in the treatment of infections with this organism. For the purpose of this study, 10 isolates from swine (9 isolates) and human (1 isolate) infected endocardium were available. Six isolates were kindly provided by A. Moca (Istituto Zooprofilattico of Perugia), and three isolates were provided by F. Foglini (Istituto Zooprofilattico of Teramo); the remaining *E. rhusiopathiae* was isolated from a patient with aortic and mitral valve endocarditis (14). All of the isolates were identified as *E. rhusiopathiae* both by standard methods (15) and by an automatic identification method (10) that includes 30 biochemical tests (Automicrobic system; Vitek Systems, Inc., Hazelwood, Mo.). The following antibiotics were kindly supplied by their manufacturers: penicillin (E. R. Squibb & Sons, Princeton, N.J.), piperacillin (Lederle Laboratories, Pearl River, N.Y.), cefotaxime and tetracycline (Hoechst Italia sud S.p.A.), imipenem (Merck Sharp & Dohme, West Point, Pa.), erythromycin (Abbott Laboratories, North Chicago, Ill.), vancomycin and daptomycin (Eli Lilly & Co., Indianapolis, Ind.), clindamycin (Pfizer Inc., New York, N.Y.), chloramphenicol (Farmitalia), trimethoprim-sulfamethoxazole (Hoffmann-La Roche Inc., Nutley, N.J.), gentamicin (Schering Corp., Bloomfield, N.J.), netilmicin (Essex), teicoplanin (Lepetit), ciprofloxacin (Bayer), and pefloxacin (Rhone-Poulenc Laboratories). Stock solutions, prepared according to the instructions of the manufacturers, were stored at −70°C until used; the exception was imipenem, stock solutions of which were prepared daily. MICs were determined by a macrodilution method in cation-supplemented Mueller-Hinton broth with 5% horse blood lysed with saponin (7). The addition of blood was required because some *E. rhusiopathiae* strains showed poor growth in Mueller-Hinton broth in preliminary testing for this study. A sample (0.5 ml) of organisms from an overnight broth culture was added to each series of tubes containing an equal volume of twofold dilutions of antibiotics to yield a final inoculum of approximately 5×10^5 organisms per ml. For each test, the inoculum size was measured by counting CFU. Tests for which the inoculum size was later found to be less than 5×10^5 CFU/ml were repeated. The MIC was defined as the lowest concentration of antibiotic that completely inhibited growth after 24 h of incubation at 35°C. The MBCs were determined by subculturing 0.01 ml of a broth culture to antibiotic-free sheep blood tryptic soy agar plates. The MBC was defined as the lowest concentration of antibiotic that exhibited 99.9% killing of the original inoculum after 48 h of incubation. The 95% confidence limit of the 99.9% killing endpoint was calculated as suggested by Pearson et al. (8). For each isolate, all MIC and MBC determinations were performed at a single time and in duplicate. American Type Culture Collection control strains (7) and *Escherichia coli* KP 1976-712 (Rhone-Poulenc) were routinely included every time the tests were performed.

Penicillin and imipenem were the most active antibiotics (Table 1); they were inhibitory or bactericidal for all isolates at concentrations of 0.01 and 0.06 μg/ml, respectively. These agents were followed by cefotaxime and piperacillin, which were bactericidal for all isolates at concentrations of 0.12 and 0.25 μg/ml, respectively. Confirming a preliminary observation on a single isolate (14), fluoroquinolones and clindamycin also proved active against *E. rhusiopathiae*. In particular, ciprofloxacin showed MIC and MBC results similar to those obtained with beta-lactam antibiotics.

The susceptibility of *E. rhusiopathiae* to vancomycin has been evaluated in seven isolates from systemic infections reported in the medical literature; all isolates are resistant to this antibiotic, as determined by disk diffusion (three isolates) or by MIC determination (four isolates) (2, 3, 12, 14). Our study seems to confirm a poor activity of vancomycin against *E. rhusiopathiae*. Six isolates, including the human strain, were inhibited by concentrations of ≥32 μg/ml, three

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TABLE 1. Comparative activities of various antibiotics against 10 isolates of *E. rhusiopathiae*[a]

Antimicrobial agent	MIC (μg/ml)			MBC (μg/ml)		
	50%	90%	Range	50%	90%	Range
Penicillin	≤0.01	≤0.01	≤0.01	0.03	0.06	≤0.01–0.06
Piperacillin	0.03	0.03	≤0.01–0.03	0.03	0.12	0.03–0.25
Cefotaxime	0.03	0.06	≤0.01–0.06	0.03	0.06	≤0.01–0.12
Imipenem	≤0.01	≤0.01	≤0.01	≤0.01	0.06	≤0.01–0.06
Erythromycin	0.06	16	0.03–32	1	≥64	0.12–≥64
Tetracycline	1	64	0.12–≥64	8	≥64	4–≥64
Chloramphenicol	0.12	64	0.01–≥64	32	≥64	8–≥64
Clindamycin	0.25	1	0.01–1	8	≥64	0.25–≥64
Gentamicin	32	≥64	4–≥64	≥64	≥64	≥64
Netilmicin	32	≥64	8–≥64	≥64	≥64	≥64
Vancomycin	32	≥64	4–≥64	≥64	≥64	32–≥64
Teicoplanin	8	16	1–32	≥64	≥64	8–≥64
Daptomycin	2	16	1–32	≥64	≥64	16–≥64
Pefloxacin	0.12	0.5	0.03–4	0.5	4	0.06–32
Ciprofloxacin	≤0.01	0.06	≤0.01–0.06	0.03	0.12	0.01–0.25
Trimethoprim-sulfamethoxazole	1.6/30.4	6.4/121	0.1/1.9–≥12.8/243	≥12.8/243	≥12.8/243	≥12.8/243

[a] 50% and 90%, MIC and MBC for 50 and 90% of isolates, respectively.

were inhibited by 8 μg/ml, and one was inhibited by 4 μg/ml; all isolates were killed by vancomycin at concentrations of ≥32 μg/ml. Teicoplanin and daptomycin appeared to be somewhat more efficacious than vancomycin; these two drugs were inhibitory for the human strain at 4 and 2 μg/ml, respectively. However, their activities appeared unsatisfactory. Erythromycin, tetracycline, and chloramphenicol were inhibitory for most of our strains. However, four isolates were inhibited by erythromycin concentrations of ≥2 μg/ml, two were inhibited by tetracycline concentrations of ≥16 μg/ml, and two were inhibited by chloramphenicol concentrations of ≥64 μg/ml. All of these resistant isolates were of animal origin. These data seem to confirm a previous observation of the emergence of *E. rhusiopathiae* strains that are resistant to the above antibiotics, possibly as a consequence of animals eating food containing antibiotics (13). As expected (2), no activity was demonstrated by trimethoprim-sulfamethoxazole and aminoglycosides.

To conclude, our study seems to confirm a satisfactory activity of penicillin against *E. rhusiopathiae*. Other beta-lactam antibiotics, imipenem, and fluoroquinolones showed activity too, whereas some resistance was observed with erythromycin, tetracycline, and chloramphenicol. More importantly, our data confirm that *E. rhusiopathiae* should be added to the list of the vancomycin-resistant gram-positive organisms (11). As previously mentioned, resistance of *E. rhusiopathiae* to vancomycin (1, 2, 12, 14) and to teicoplanin (14) may be of some interest, because these agents have been recommended for endocarditis patients who are allergic to penicillin and infected with a gram-positive organism (4–6, 16). In particular, vancomycin plus an aminoglycoside is frequently recommended in the empiric therapy of acute prosthetic valve endocarditis (17). Systemic infection with *E. rhusiopathiae* may be fulminant (2, 12, 14) and frequently associated with endocardium involvement (2). Recently, a case of *E. rhusiopathiae* infection of an aortic valve prosthesis was reported (3). Thus, it appears advisable to consider antibiotics other than vancomycin in the event of acute endocarditis developing in individuals who report a skin lesion suggestive of erysipeloid and/or who have occupational risk factors. Based on data from the present study, use of fluoroquinolones may considered in *E. rhusiopathiae* infections when beta-lactam administration is contraindicated (e.g., beta-lactam allergy).

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