

Past administration of β -lactam antibiotics and increase in the emergence of β -lactamase-producing bacteria in patients with orofacial odontogenic infections.

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The past administration of β -lactam antibiotics increases the emergence of β -lactamase-producing bacteria in patients with orofacial odontogenic infections

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1 **ABSTRACT**

2 *Objectives.* The purpose of this study was to determine the current status of β -
3 lactamase-producing bacteria in orofacial odontogenic infections.

4 *Study design.* Microbiological data from pus specimens of 111 cases with
5 orofacial odontogenic infections were analyzed in relation to the past
6 administration of β -lactams in the enrolled infections.

7 *Results.* β -lactamase-producing bacteria were isolated more frequently from the
8 β -lactam-administered group (38.5%) than from the β -lactam-nonadministered
9 group (10.9%) ($P < .005$), and they were isolated more frequently as the duration
10 of administration increased. The predominant bacteria isolated included
11 *Prevotella*, the most frequent isolate, viridans streptococci, *Peptostreptococcus*,
12 and *Fusobacterium*, and 7.1% of total isolates produced β -lactamase. Penicillin
13 and cefazolin worked well with β -lactamase-nonproducing *Prevotella*, but were
14 remarkably affected by β -lactamase-producing *Prevotella*. Cefmetazole,
15 sulbactam/cefoperazone, and imipenem worked well against both kinds of
16 *Prevotella*.

17 *Conclusions.* β -lactams are still suitable for the first antimicrobial therapy in the
18 treatment of the infections. However, since past β -lactam administration
19 increases the emergence of β -lactamase-producing bacteria, β -lactamase-stable
20 antibiotics should be prescribed to patients with unresolved infections who have
21 received β -lactams.

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1 For the treatment of orofacial odontogenic infections, the β -lactam antibiotics
2 are recommended because they work well against the specific bacterial causative
3 agents of orofacial odontogenic infections with a very low incidence of adverse
4 effects.¹⁻⁶ Additionally, treatment with β -lactam antibiotics is cost-effective. A
5 problem with antimicrobial therapy with β -lactams is the increasing rates of β -
6 lactam resistance, which lead to treatment failures.³⁻⁶ β -lactam resistance is
7 considered to be closely correlated with the emergence of β -lactamase producing
8 bacteria.³⁻⁹ There have been many reviews of orofacial odontogenic infections
9 stressing the importance of β -lactamase-producing bacteria in β -lactam
10 resistance.³⁻⁶ Surprisingly, however, very little data regarding the occurrence of
11 β -lactamase-producing bacteria in orofacial odontogenic infections, on which the
12 reviews should be based, is available. Most of the examinations of β -lactamase-
13 producing bacteria have been limited to a few bacterial species or to periodontal
14 disease.¹⁰⁻¹⁴ We therefore determined that data regarding the current status of
15 the occurrence of β -lactamase-producing bacteria in orofacial odontogenic
16 infections were required.

17 Purulent orofacial odontogenic infections can be managed by tooth extraction,
18 endodontic therapy, and surgical treatment, including drainage, without the use
19 of antibiotics.^{1,3-5} However, when acute bacterial infection has progressed, or
20 when antimicrobial therapy might benefit patients, antibiotics are prescribed. In
21 Japan, when acute odontogenic infections except pulpitis and gingivitis simplex
22 are diagnosed or strongly suspected, almost all oral surgeons prescribe
23 antibiotics in the course of the treatment to ensure the efficacy of treatment, or
24 to minimize the risk of infection progression.

1 In Japan, oral surgeons in large hospitals and medical centers are often referred
2 the patients with unsolved infections from other oral surgeons or doctors. The
3 oral surgeons should take into account the past administration of antibiotics for
4 orofacial odontogenic infections. To effectively administer antimicrobial
5 therapy for patients, microbiological data from an individual pus specimen must
6 be obtained. Generally, however, it takes several days or longer to obtain the
7 necessary data, and we therefore frequently start empiric antimicrobial therapy.
8 For this reason, it is necessary to establish a principle regimen of empiric
9 antimicrobial therapy for orofacial odontogenic infections, including cases
10 treated with antibiotics in the past.

11 To address these issues, we investigated the relationships between the past
12 administration of β -lactam antibiotics, the emergence of β -lactamase-producing
13 pathogens, and the antimicrobial susceptibility of the isolates from pus
14 specimens of orofacial odontogenic infections. Our results show that *Prevotella*
15 has the highest incidence of β -lactamase production in frequent isolates, and that
16 the past administration of β -lactam antibiotics increases the isolation of β -
17 lactamase-producing bacteria. Furthermore, based on the results, we discuss a
18 regimen of antimicrobial chemotherapy for the effective treatment of orofacial
19 odontogenic infections.

20

21 **MATERIAL AND METHODS**

22 **Patients**

23 The case histories of a total of 111 patients with obstructed abscesses caused by
24 orofacial odontogenic infections were investigated. All patients were treated at
25 our hospital during the 48 months between January 1993 and December 1996.

1 Patients who required serious medical care (e.g., cases with diabetes mellitus,
2 rheumatoid arthritis, respiratory tract infections, leukemia) were excluded. The
3 types of infection observed were dentoalveolar infections, 95 cases;
4 periodontitis, 8 cases; and pericoronitis, 8 cases.

5 The subjects were classified into two groups: the β -lactam (+) group and the β -
6 lactam (-) group. The former had received β -lactam antibiotics for the treatment
7 of orofacial odontogenic infections prior to the pus collection for this study. The
8 administration of β -lactams had occurred once in the course of the infection
9 within 8 days prior to the pus collection. The patients had received only β -
10 lactam antibiotics during the course of their infections and had not been
11 administered any additional antibiotics within the previous 3 months. A total of
12 65 cases belonged to the β -lactam (+) group. The types of infection included
13 were dentoalveolar infections, 56 cases; periodontitis, five cases; and
14 pericoronitis, four cases. The average age of this group was 40.3 years (range 7-
15 77 years). β -lactam antibiotics were prescribed to 47 patients in our hospital,
16 and to 18 patients at other hospitals and private practices. The β -lactam
17 antibiotics administered to the patients were oral-penicillin, four cases;
18 intravenous-penicillin, two cases; oral-first-generation cephalosporin, six cases;
19 intravenous-first-generation cephalosporin, one case; intravenous-second-
20 generation cephalosporin, 21 cases; oral-third-generation cephalosporin, 27
21 cases; intravenous-third-generation cephalosporin, two cases; and carbapenem,
22 two cases. The appropriateness of the use of antibiotics, including the dose and
23 duration, was confirmed by the authors. The other group was the β -lactam (-)
24 group, who had not received any antibiotics within 3 months prior to the pus
25 collection for this study. Forty-six cases belonged to the β -lactam (-) group.

1 The average age was 48.7 years (range 18-85 years). The types of infection
2 included were dentoalveolar infections, 39 cases; periodontitis, three cases;
3 pericoronitis, four cases. Information regarding the past and physical histories
4 of the patients were obtained by interview and from the medial records of our
5 hospital, if they existed. When patients were treated for orofacial odontogenic
6 infections by doctors other than the authors, we interviewed the doctors
7 regarding the patient histories.

8 This study was performed based on the permission of all patients who
9 participated.

10

11 **Bacterial quantitative examination**

12 The pus specimens were collected from the abscesses by aspiration with an 18-
13 gauge needle. The specimens were placed in anaerobic transport devices (Seed
14 Tube; Eiken, Tokyo, Japan) and immediately transported to the laboratory. The
15 specimens were incubated on Brucella HK agar (Kyokuto, Tokyo, Japan) with
16 5% sheep blood in an atmosphere of 5% CO₂, 10% H₂, and 85% N₂ at 37°C for
17 78 h. At the same time, the same specimens were aerobically incubated on
18 Brucella HK agar with 5% sheep blood, and on the same agar in an atmosphere
19 of 10% CO₂, 20% H₂, and 70% N₂ at 37°C for 48 h. Even when no bacteria
20 growth was observed, incubation was continued for at least 7 days. Anaerobic
21 bacteria were identified using Rap ID ANA II (Innovative Diagnostic System,
22 Norcross, GA). In addition to this test, gas liquid chromatography was
23 performed as needed to identify bacteria.¹⁵ Aerobic and micro-aerophilic
24 bacteria were identified using conventional methods.¹⁶ Bacterial strains were
25 stored in 10% skim milk (Difco, Detroit, MA) at -80°C.

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2 **β-lactamase test**

3 Nitrocefin disks (Cefinase disk; BBL Microbiology Systems, Cockeysville,
4 MD) were inoculated with a small portion of growth from the Brucella blood
5 agar plates described above and observed for a change in color from yellow to
6 red.¹⁷

7

8 **Susceptibility test**

9 Antibiotics were obtained from their manufacturers as laboratory powders, each
10 of a defined potency: penicillin G (Banyu, Tokyo, Japan), ampicillin (Meiji,
11 Tokyo, Japan), cefazolin (Fujisawa, Tokyo, Japan), cefmetazole (Sankyo, Tokyo,
12 Japan), sulbactam/cefoperazone (Pfizer, Tokyo, Japan), and imipenem (Banyu).
13 All minimum inhibitory concentrations (MICs) were determined by the agar
14 dilution method recommended by the National Committee for Clinical
15 Laboratory standards¹⁸; the MICs of anaerobes were determined using the
16 Brucella HK agar with 5% sheep blood in an atmosphere of 5% CO₂, 10% H₂,
17 and 85% N₂ at 37°C for 48 h. The susceptibility breakpoints were determined on
18 the basis of the propositions of the National Committee for Clinical Laboratory
19 standards¹⁸; the breakpoints used were 2.0 μg/ml for penicillin G and ampicillin,
20 8.0 μg/ml for cefazolin, 16.0 μg/ml for cefmetazole and sulbactam/cefoperazone,
21 and 4.0 μg/ml for imipenem.

22

23 **Statistical analysis**

24 Statistical comparisons of the incidence of β-lactamase-producing bacteria and
25 susceptibility rate in the susceptibility test were performed by a χ^2 test.

1

2 **RESULTS**

3 β -lactamase-producing bacteria were isolated in 25 of 65 cases (38.5%) in the
4 β -lactam (+) group, while in only five of 46 cases (10.9%) in the β -lactam (-)
5 group. The incidence of the isolation of β -lactamase-positive bacteria in the β -
6 lactam (+) group was significantly higher than in the β -lactam (-) group (P
7 $< .005$) (Table I). Furthermore, we found a correlation between the incidence of
8 the isolation of β -lactamase-producing bacteria and the duration of the past
9 administration of β -lactams (Table I). The incidence of isolation of β -lactamase-
10 producing bacteria was low in the patients who had received β -lactam for 1 or 2
11 days. However, as the administration duration increased, β -lactamase-producing
12 bacteria were isolated more frequently. It is interesting that both patients who
13 received β -lactam for 8 days had β -lactamase-producing bacteria.

14 A total of 449 strains of bacteria were isolated from the 111 cases (Table II).
15 Out of a total of 449 isolates, 32 (7.1%) were β -lactamase-positive strains.
16 Twenty-nine of 266 isolates (10.9%) and three of 183 isolates (1.6%) were β -
17 lactamase-producing bacteria in the β -lactam (+) and in the β -lactam (-) groups,
18 respectively. This difference was significant ($P < .001$). A distinct difference in
19 the variety of bacterial species isolated between the β -lactam (+) and β -lactam (-)
20 groups was not observed. *Prevotella*, viridans streptococci, *Peptostreptococcus*,
21 and *Fusobacterium* were isolated frequently (Table II). In the isolated
22 organisms, β -lactamase-producing strains were detected in *Enterobacter*,
23 *Klebsiella*, *Prevotella*, *Porphyromonas*, and *Bacteroides*, but no strains of the
24 other species produced β -lactamase. All isolates of *Enterobacter* and *Klebsiella*
25 produced β -lactamase, but these species were rarely isolated. The pigmented

1 *Prevotella* (*P. intermedia*, *P. melaninogenica*, and *P. loescheii*) and
2 nonpigmented *Prevotella* (*P. oralis*, *P. oris*, and *P. buccae*) were isolated
3 frequently, and a significant number of these isolates produced β -lactamase:
4 27.3% (18 of 66) of pigmented *Prevotella* strains and 16.7% (7 of 42) of
5 nonpigmented *Prevotella* strains were β -lactamase positive. β -lactamase-
6 producing strains of pigmented *Prevotella*, nonpigmented *Prevotella*, and
7 *Bacteroides* were often found in the β -lactam (+) group. In particular, β -
8 lactamase-producing strains of *P. intermedia* were isolated more frequently from
9 the β -lactam (+) group than from the β -lactam (-) group with a significance of P
10 $< .05$.

11 β -lactamase-producing bacteria were detected in two of four cases receiving
12 oral-penicillin, in one of two cases received intravenous-penicillin, in four of six
13 cases receiving oral-first-generation cephalosporin, in one of one cases receiving
14 intravenous-first generation cephalosporins, in five of 21 cases receiving
15 intravenous-second generation cephalosporin, in 11 of 27 cases receiving oral
16 third-generation cephalosporin, in zero of two cases receiving intravenous-third
17 generation cephalosporin, and in one of two cases receiving intravenous
18 carbapenem.

19 Since *Prevotella* was isolated frequently and showed a high incidence of β -
20 lactamase production (Table II), the antimicrobial susceptibility of *Prevotella* to
21 several β -lactam antibiotics was determined (Table III). In both pigmented
22 *Prevotella* and nonpigmented *Prevotella*, the MIC (MIC₅₀ and MIC₉₀) values of
23 penicillin G, ampicillin, and cefazolin of β -lactamase-producing strains were
24 distinctly greater than those of the nonproducing strains. In addition, the
25 susceptibility rates of β -lactamase-producing strains in pigmented and

1 nonpigmented *Prevotella* were significantly smaller than those of the
2 nonproducing strains ($P < .03$). The MIC values of cefmetazole and
3 sulbactam/cefoperazone of the β -lactamase-producing strains in pigmented
4 *Prevotella* were also higher than those of the non β -lactamase-producing strains,
5 but all strains were susceptible to cefmetazole and sulbactam/cefoperazone. In
6 nonpigmented *Prevotella*, there were little differences in the MIC values of
7 cefmetazole and sulbactam/cefoperazone between β -lactamase-producing and
8 nonproducing strains, and all strains were susceptible to them. Imipenem had
9 quite low MIC values and high susceptibility rates against both pigmented and
10 nonpigmented *Prevotella*, but there were no strict differences in MIC values or
11 susceptibility rates between β -lactamase-producing strains and nonproducing
12 strains of both pigmented and nonpigmented *Prevotella*.

13

14 **DISCUSSION**

15 In Japan, the use of antibiotics in oral surgery is strictly regulated by the
16 Ministry of Health and Welfare of Japan via the national health insurance.¹⁹ The
17 costs of exceeded dose and incorrect selection of antibiotics are billed to the
18 hospitals employing the oral surgeons who prescribed them, or to the surgeons
19 themselves if they are owners of clinics. Thus, to our knowledge, remarkably
20 inappropriate use of antibiotics for the treatment of orofacial odontogenic
21 infections is rare in Japan, although there would be differences concerning the
22 management of antibiotic therapy between nations.

23 Three modes of resistance to β -lactam antibiotics have been proposed regarding
24 pathogens of the orofacial odontogenic infection: β -lactamase production,
25 barriers to target sites, and penicillin-binding proteins.^{7,20} β -lactamase

1 production would protect not only β -lactamase-producing bacteria but also the
2 nonproducing bacteria from β -lactam antibiotics²¹⁻²³: because orofacial
3 odontogenic infections are polymicrobial,^{2,4-6,24} the emergence of β -lactamase-
4 producing bacteria may protect the nonproducing bacteria from the β -lactam
5 antibiotics. It is well known that staphylococcal organisms and some gram-
6 negative bacilli can produce β -lactamase.²⁵⁻²⁸ In the present study, β -lactamase
7 was detected in aerobic and strictly anaerobic gram-negative bacilli, while none
8 of the *Staphylococcus* isolated produced this enzyme. The incidence of β -
9 lactamase-producing anaerobic gram-negative bacilli has been reported in
10 several studies.^{10-12,17} β -lactamase is detected in 26% to 100% of pigmented
11 *Prevotella* involving *P. intermedia*, *P. melaninogenica*, *P. loescheii*,^{10,17} 37.5%
12 to 77.1% of nonpigmented *Prevotella*,^{10,12} 13% to 23.5% of *F. nucleatum*,^{11,12,17}
13 and 33.3% of *P. gingivalis*.¹² In the present study, 27.3% of pigmented
14 *Prevotella*, 16.7% of nonpigmented *Prevotella*, 0% of *Fusobacterium*, and only
15 one strain of *Porphyromonas* produced β -lactamase. The incidence of β -
16 lactamase-producing bacteria observed in this study was lower than that of
17 previous studies.

18 β -lactamase-producing bacteria resist antimicrobial chemotherapy with
19 penicillins.^{3-7,22} In addition, β -lactamase produced by *P. melaninogenica* and *P.*
20 *oralis* have been shown to be more active against penicillins than against
21 cephalosporins.⁷ Cefazolin is a first- generation cephalosporin.²⁹ In general,
22 the first-generation cephalosporins are affected by β -lactamase more strongly
23 than the second- or third- generation agents. Cefmetazole is stable with β -
24 lactamase and active against anaerobic bacteria.^{30,31} Sulbactam/cefoperazone is
25 a member of the cephalosporin family made by combining cefoperazone and

1 sulbactam, a β -lactamase inhibitor.³² Adding sulbactam to β -lactam antibiotics
2 has been shown to increase antibacterial activity against β -lactamase-producing
3 bacteria.^{7,32-34} Imipenem has an unusually broad spectrum, a high potency, a
4 stability to β -lactamase, and no cross-resistance with other β -lactam agents.³⁴⁻³⁶
5 It is interesting that the activity of test penicillins and cefazolin against β -
6 lactamase-producing *Prevotella* was decreased remarkably in the present study,
7 while these antibiotics inhibited the growth of the β -lactamase-nonproducing
8 *Prevotella*. In contrast, cefmetazole and sulbactam/cefoperazone were active
9 against both β -lactamase-producing and nonproducing *Prevotella*. Moreover,
10 imipenem greatly inhibited the growth of β -lactamase-producing *Prevotella*.

11 In penicillin therapy, the relationship between exposure to penicillin and the
12 emergence of β -lactamase-producing bacteria has been discussed.^{13,14,37} Brook
13 et al³⁷, Heimdahl et al¹³, and Kinder et al¹⁴ have noted that the use of
14 penicillin is associated with the emergence of β -lactamase-producing bacteria,
15 while the work of Lewis et al²² does not support this conclusion. In the present
16 study, although cephalosporins were administered more frequently than
17 penicillins, β -lactamase-producing bacteria were found more frequently in the β -
18 lactam (+) group than in the β -lactam (-) group. Especially in *Prevotella*, which
19 was the most frequent isolate, β -lactamase-producing strains were found more
20 frequently in the β -lactam (+) group than in the β -lactam (-) group. This
21 suggests that past antimicrobial therapy with β -lactam antibiotics for an
22 unresolving infection increases the incidence of β -lactamase-producing bacteria
23 in abscesses of odontogenic infections.

24 We found an interesting correlation between the incidence of β -lactamase-
25 producing bacteria and the duration of β -lactam administration in the past

1 treatment in orofacial odontogenic infections. When the duration was 1 or 2
2 days, few β -lactamase-producing bacteria emerged. However, when patients
3 received β -lactam antibiotics for 3 days or more, 50% or more of the cases
4 acquired β -lactamase-producing bacteria. In Japan, the daily doses of β -lactams
5 usually used for adult orofacial odontogenic infections are regulated by Health
6 and Welfare of Japan. For example, the doses for an adult (with 60 kg weight)
7 are as follows: oral-ampicillin, 1 g; intravenous-ampicillin, 2 g; cephalexin, 750
8 mg; cefazolin, 1 g; cefmetazole, 2 g; cefpodoxime, 200 mg; cefdinir, 300 mg.¹⁹
9 All patients in the β -lactam (+) group received the appropriate doses. A clear
10 correlation between the incidence of β -lactamase-producing bacteria and the type
11 of antibiotics or route of administration was not found. Further studies to
12 evaluate the relations between the incidence of β -lactamase-producing bacteria
13 and the type of antibiotics, dosage, or route of administration may be required
14 based on both the patient population and the microbiological population.
15 However, the present study suggests that if patients with orofacial odontogenic
16 infections have already received β -lactam antibiotics for 3 days or more,
17 regardless of the type of antibiotic or the route of administration, we should
18 assume that β -lactamase-producing bacteria are present in the lesion and are
19 associated with infection progression.

20 Based on this study, we propose a principle for developing a regimen to treat
21 orofacial odontogenic infections empirically. If the patients have not received β -
22 lactam antibiotics in the course of the infections, or even if they have received β -
23 lactam antibiotics with an appropriate dose for a duration of 1 day or 2 days,
24 penicillins and primitive cephalosporins are suitable to prescribe, since in this
25 instance there is only a small possibility of the occurrence of β -lactamase-

1 producing bacteria, and these antibiotics are considered to be effective. In
2 contrast, if the patients already received antimicrobial therapy with β -lactams in
3 the course of the infections for a duration of 3 days or more, it should be
4 assumed that β -lactamase-producing bacteria may occur or be present in the
5 unsolving lesion. In such cases, β -lactamase-stable β -lactams or non- β -lactam
6 antibiotics such as clindamycin and macrolide may be effective.^{1-6,38,39} In this
7 case, we recommend the primary use of β -lactamase-stable β -lactams, since they
8 have great effectiveness against pathogens of the infection, especially
9 *Prevotella*, *Porphyromonas*, and *Fusobacterium*,^{33,34} and the occurrence of side
10 effects is lower than with other antibiotics. In addition, cost should be taken into
11 account. Many of these β -lactamase-stable antibiotics are more expensive than
12 penicillins and primitive cephalosporins.^{5,40} For example, in Japan, the costs of
13 cefmetazole, sulbactam/cefoperazone, and imipenem are two to five times as
14 high as the cost of penicillins or primitive cephalosporins. Moreover, to prevent
15 increasing the incidence of resistance to these β -lactamase-stable agents, they
16 should not be abused. Therefore, we do not agree with the practice of
17 prescribing β -lactamase-stable antibiotics to all patients without consideration.
18 Not only *Prevotella* but also viridans streptococci, *Peptostreptococcus*, and
19 *Fusobacterium* have been shown to be frequent isolates in orofacial odontogenic
20 infections.^{2,4,24,41} The resistance mechanisms of viridans streptococci and
21 *Peptostreptococcus* against β -lactams are rather to alter membrane permeability
22 or to alter target sites (the mutation of penicillin-binding proteins) than to induce
23 β -lactamase production.^{42,43} However, the regimen proposed here would be
24 effective against these bacteria, including *Fusobacterium*, based on the
25 susceptibility data of other studies^{12,44-46} and our unpublished data. Our

1 department now employs this regimen, and satisfactory results are being obtained
2 (unpublished data).

3 The results of this study and the regimen proposed here may be helpful in
4 devising a more effective treatment for orofacial odontogenic infections.

5

6

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Table I. Correlation between the incidence of β -lactamase-producing bacteria and the β -lactam-administered duration in past antimicrobial treatment

<i>Group*</i>	<i>Duration (days)</i>	<i>Incidence[†]</i>
β -lactum (-)	No administration	5/46 (10.9)
β -lactum (+)	1	0/ 7
	2	2/14 (14.3)
	3	15/30 (50.0)
	4	2/ 4 (50.0)
	5	2/ 4 (50.0)
	6	2/ 4 (50.0)
	7	0/ 0
	8	2/ 2 (100)

*See the text regarding this grouping.

[†]No. of cases from which β -lactamase -producing bacteria were isolated / No. of total cases (percents).

Table II. Incidence of β -lactamase-producing bacteria from patients with orofacial odontogenic infections

<i>Aerobes</i>	<i>Incidence</i> *		<i>Anaerobes</i>	<i>Incidence</i> *	
	β -lactam (+) group †	β -lactam (-) group ‡		β -lactam (+) Group †	β -lactam (-) group ‡
Viridans streptococci	0/49	0/38	<i>Peptostreptococcus</i>	0/44	0/29
<i>Staphylococcus</i>	0/ 2	0/ 1	<i>Gemella</i>	0/16	0/ 9
<i>Micrococcus</i>	0/ 1	0/ 0	<i>Eubacterium</i>	0/ 1	0/ 5
<i>Corynebacterium</i>	0/ 1	0/ 3	Pigmented <i>Prevotella</i>	17/47 (36.2)	1/19 (5.3)
<i>Lactobacillus</i>	0/ 3	0/ 2	<i>P. intermedia</i>	12/30 (40.0) §	1/14 (7.1)
<i>Actinomyces</i>	0/ 1	0/ 3	<i>P. melaninogenica</i>	4/ 7 (57.1)	0/ 2
<i>Neisseria</i>	0/ 1	0/ 1	<i>P. loescheii</i>	1/10 (10.0)	0/ 3
<i>Klebsiella</i>	1/ 1 (100)	0 / 0	Nonpigmented <i>Prevotella</i>	6/24 (25.0)	1/18 (5.6)
<i>Enterobacter</i>	2/ 2 (100)	0/ 0	<i>P. oralis</i>	4/ 9 (44.4)	1/ 7 (14.3)
<i>Campylobacter</i>	0/ 3	0/ 3	<i>P. oris</i>	1/ 6 (16.7)	0/ 3
Unidentified aerobes	0/ 4	0/ 3	<i>P. buccae</i>	1/ 9 (11.1)	0/ 8
			<i>Porphyromonas gingivalis</i>	0/10	0/12
			<i>P. endodontalis</i>	0/ 1	1/ 3 (33.3)
			<i>Fusobacterium nucleatum</i>	0/33	0/21
			<i>F. necrophorum</i>	0/ 5	0/ 5
			<i>Bacteroides</i>	3/ 9 (33.3)	0/ 2
			<i>Veillonella</i>	0/ 2	0/ 1
			Unidentified anaerobes	0/ 6	0/ 5
Total	3/ 68 (4.4)	0/ 54	Total	26/ 198 (13.1) §	3/ 129 (2.3)

*No. of β -lactamase-producing isolates / No. of total isolates (percents).

†,‡ See the text regarding this grouping.

§ Statistically significant at $P < .05$.

Table III. Antimicrobial susceptibility of *Prevotella* against β -lactam antibiotics

	<i>β-lactamase-producing strains</i>			<i>β-lactamase-nonproducing strains</i>		
	<i>MIC ($\mu\text{g/ml}$)</i>		<i>Susceptibility rate(%)</i>	<i>MIC ($\mu\text{g/ml}$)</i>		<i>Susceptibility rate(%)</i>
	<i>50%</i>	<i>90%</i>		<i>50%</i>	<i>90%</i>	
Pigmented <i>Prevotella</i>						
Penicillin G	4.0	32.0	33.3 *	≤ 0.015	2.0	87.5
Ampicillin	0.5	64.0	61.1 *	0.06	0.5	93.8
Cefazolin	2.0	16.0	83.3 *	≤ 0.015	0.5	100
Cefmetazole	0.5	2.0	100	≤ 0.015	1.0	100
Sulbactam/ cefoperazone	1.0	8.0	100	≤ 0.015	1.0	100
Imipenem	≤ 0.015	0.06	100	≤ 0.015	0.06	100
Non-pigmented <i>Prevotella</i>						
Penicillin G	16.0	32.0	0.0 *	0.06	0.5	100
Ampicillin	16.0	32.0	0.0 *	0.1	2.0	82.9
Cefazolin	16.0	64.0	28.6 *	0.1	1.0	100
Cefmetazole	4.0	4.0	100	0.2	8.0	100
Sulbactam/ cefoperazone	2.0	2.0	100	0.5	8.0	100
Imipenem	≤ 0.015	0.06	100	0.06	0.2	100

In pigmented *Prevotella*, 18 β -lactamase-producing strains and 48 β -lactamase nonproducing strains were tested. In nonpigmented *Prevotella*, seven β -lactamase-producing strains and 35 β -lactamase-nonproducing strains were tested.

* $P < .03$ vs. β -lactamase-nonproducing strains.