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## **Bacteriologic features and antimicrobial susceptibility in isolates from orofacial odontogenic infections**

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1 **Abstract**

2 **Objective.** The aim of this study is to obtain helpful information for an effective  
3 antimicrobial therapy against orofacial odontogenic infections; such information  
4 would be obtained from recent bacteriologic features and antimicrobial susceptibility  
5 data.

6 **Study design.** The bacteriology and antimicrobial susceptibility of major pathogens  
7 in 163 patients with orofacial odontogenic infections to seven antibiotics was  
8 examined.

9 **Results.** Mixed infection of strict anaerobes with facultative anaerobes (especially  
10 viridans streptococci) was observed most often in dentoalveolar infections,  
11 periodontitis, and pericoronitis. Penicillin (penicillin G) was effective against  
12 almost all pathogens, although it did not work well against  $\beta$ -lactamase-positive  
13 *Prevotella*. Cefmetazole was effective against all test pathogens. Erythromycin  
14 was ineffective against viridans streptococci and most *Fusobacterium*. Clindamycin  
15 exerted a strong antimicrobial activity on anaerobes. Minocycline was effective  
16 against almost all of the test pathogens. The antimicrobial activity of levofloxacin  
17 against viridans streptococci was not strong.

18 **Conclusions.** An antibiotic that possesses antimicrobial activity against both  
19 viridans streptococci and oral anaerobes should be suitable for treatment of  
20 dentoalveolar infection, periodontitis, and pericoronitis. Penicillin remains effective  
21 as an antimicrobial against most major pathogens in orofacial odontogenic infections.  
22 Cefmetazole, clindamycin, and minocycline may be effective against most pathogens,  
23 including penicillin-unsusceptible bacteria.

1 Although numerous patients suffer from orofacial odontogenic infections, many of  
2 these infections can be managed without the use of antibiotics, e.g., by tooth  
3 extraction, endodontic therapy, and surgical treatment, including drainage.<sup>1-6</sup>  
4 However, when an acute bacterial infection has progressed or antimicrobial therapy  
5 might be of benefit to patients, antibiotics are prescribed.<sup>1-6</sup> When antibiotics are  
6 prescribed for the treatment of orofacial odontogenic infections, clinicians should  
7 choose them on a case-specific basis, and the choice should be based on several  
8 factors, e.g., laboratory data, patient's health, age, allergies, drug absorption and  
9 distribution ability, and plasma levels.<sup>1-6</sup> Penetration and metabolism of the drug,  
10 type or location of the infection, previous use of antibiotics, and cost are other factors  
11 to be considered.<sup>1-6</sup> The laboratory data regarding bacteriology and antimicrobial  
12 susceptibility is crucial information for the clinician considering the administration of  
13 the antimicrobial therapy.<sup>3,6,7-9</sup> However, it may take several days or even longer to  
14 obtain such data. Hence, antibiotics may be chosen empirically.  $\beta$ -Lactam  
15 antibiotics, especially penicillins, have traditionally been recommended as a first-line  
16 antibiotic because they work well against most causative bacteria and because  
17 penicillins have a low incidence of side effects.<sup>1-6</sup> Furthermore, such medicines are  
18 relatively inexpensive.<sup>3,6</sup> Some studies have suggested that the antimicrobial  
19 activity of penicillins has decreased against the causative bacteria related to orofacial  
20 odontogenic infections, such as streptococci and oral anaerobes.<sup>1,4-6</sup> However, the  
21 debate continues over whether penicillins remain adequate as the first-line antibiotics  
22 of choice.<sup>1-7</sup> Alternative regimens of antimicrobial therapy have been proposed for  
23 patients with penicillin allergies, or in cases in which penicillin therapy has failed.<sup>2-6</sup>  
24 In addition, the properties of each antibiotic therapy should be considered based on  
25 up-to-date information about domestic antimicrobial susceptibility.

1 In the present study, the bacteriological features of orofacial odontogenic infections  
2 and the antimicrobial susceptibility of pathogens recently isolated at our hospital were  
3 determined. Based on the data, we estimated the antimicrobial effectiveness of each  
4 antibiotic as regards the treatment of orofacial odontogenic infections.

5

## 6 **MATERIALS AND METHODS**

### 7 **Patients**

8 The case histories of a total of 163 patients with obstructed abscesses caused by  
9 orofacial odontogenic infections were investigated. The patients were treated at our  
10 hospital between April 1991 and March 1997. Patients who required intensive  
11 medical care (e.g., cases with diabetes mellitus, rheumatoid arthritis, respiratory tract  
12 infections, leukaemia) were excluded. The following orofacial odontogenic  
13 infections were studied: dentoalveolar infections (128 cases), periodontitis (24 cases),  
14 and pericoronitis (11 cases). Before pus collection, at our hospital, other hospitals,  
15 or private practices, ninety-one patients had received antibiotics ( $\beta$ -lactam antibiotics)  
16 during the course of the infection.

17 All subjects in this study gave their informed consent to participate.

18

### 19 **Bacteriologic examination**

20 To identify causative agents, pus specimens were sampled. The specimens were  
21 collected from the abscesses with an 18-gauge needle. The specimens were placed  
22 in anaerobic transport devices (Seed Tube; Eiken, Tokyo, Japan) and were  
23 immediately transported to the laboratory.

24 When the specimens reached the laboratory, bacteriologic examination was  
25 performed immediately as follows: a portion of each specimen was incubated on

1 Brucella HK agar (Kyokuto, Tokyo, Japan) with 5% sheep blood in an atmosphere of  
2 5% CO<sub>2</sub>, 10% H<sub>2</sub>, and 85% N<sub>2</sub> at 37°C for 78 h. At the same time, a portion of the  
3 specimen was also incubated on Brucella HK agars with 5% sheep blood in an aerobic  
4 atmosphere and in an atmosphere of 10% CO<sub>2</sub>, 20% H<sub>2</sub>, and 70% N<sub>2</sub> at 37°C for 48 h.  
5 Incubation continued for at least seven days, even in the absence of bacterial growth.  
6 Aerobic and micro-aerophilic bacteria were identified using conventional  
7 methods.<sup>10,11</sup> Anaerobic bacteria were identified using Rap ID ANA II (Innovative  
8 Diagnostic System, Norcross, GA). In addition to the test, gas liquid  
9 chromatography was performed when needed to identify the bacteria.<sup>11,12</sup> After the  
10 bacteriologic examination, bacterial strains were stored in 10% skim milk  
11 (Becton-Dickinson, Cockeysville, MD) at -80°C until the susceptibility test could be  
12 performed.

13

#### 14 **Susceptibility test**

15 Antibiotics were obtained from their manufacturers as laboratory powders; each  
16 antibiotic was of a defined potency: penicillin G (Banyu, Tokyo, Japan), cefazolin  
17 (Fujisawa, Osaka, Japan), cefmetazole (Sankyo, Tokyo, Japan), erythromycin  
18 (Shionogi, Osaka, Japan), clindamycin (Pharmacia & Upjohn, North Peapack, NJ),  
19 minocycline (Takeda, Osaka, Japan), and levofloxacin (Dai-ichi, Tokyo, Japan).

20 All minimum inhibitory concentrations (MICs) were determined by the agar  
21 dilution method recommended by the National Committee for Clinical Laboratory  
22 Standards (NCCLS).<sup>7,8</sup> The MICs of streptococci were determined using  
23 Mueller-Hinton agar (Becton Dickinson) with 5% sheep blood in an atmosphere of  
24 10% CO<sub>2</sub>, 20% H<sub>2</sub>, and 70% N<sub>2</sub> at 37°C for 24 h.<sup>7</sup> A reference strain of  
25 *Streptococcus pneumoniae* ATCC 49619 was used as the control in each test.<sup>7</sup> The

1 MICs of anaerobes were determined using Brucella HK agar with 5% sheep blood in  
2 an atmosphere of 5% CO<sub>2</sub>, 10% H<sub>2</sub>, and 85% N<sub>2</sub> at 37°C for 48 h.<sup>8</sup> Reference  
3 strains of *Bacteroides fragilis* ATCC 25285 and *Bacteroides thetaiotaomicron* ATCC  
4 29741 were used as controls in each test.<sup>8</sup> In the present study, the susceptibility  
5 breakpoints against viridans streptococci and anaerobes were determined by NCCLS  
6 criteria.<sup>7-9</sup> Since the breakpoints of cefazolin, minocycline, and levofloxacin against  
7 anaerobes have not been determined by the NCCLS, we determined them based on the  
8 breakpoints of other similar antibiotics, i.e., those which resemble them in structure  
9 and pharmacokinetics. The breakpoints against viridans streptococci were as  
10 follows: penicillin G, ≤0.12µg/ml; cefazolin, ≤8µg/ml; cefmetazole, ≤8µg/ml;  
11 erythromycin and clindamycin, ≤0.25µg/ml; minocycline, ≤2µg/ml; levofloxacin,  
12 ≤2µg/ml. The breakpoints against strict anaerobes were as follow: penicillin G,  
13 ≤0.5µg/ml; cefazolin, ≤8µg/ml; cefmetazole, ≤16µg/ml; clindamycin, ≤2µg/ml;  
14 minocycline, ≤4µg/ml; levofloxacin, ≤2µg/ml. As the breakpoint of erythromycin  
15 against strict anaerobes has not been determined by the NCCLS, it was determined for  
16 the present study to be ≤4µg/ml, according to a report by Spangler *et al.*<sup>13</sup>

17

### 18 **β-Lactamase test**

19 Nitrocefin disks (Cefinase disk; Becton Dickinson) were inoculated as described  
20 above with a small portion of growth from the Brucella blood agar plates and the  
21 disks were observed for a change in colour from yellow to red.<sup>6,14</sup> *Bacteroides*  
22 *fragilis* ATCC 25285 was included as a positive control.<sup>14</sup>

23

### 24 **Correlation of antimicrobial activity of penicillin G with that of other antibiotics**

25 The strains of each pathogen were divided into two groups. When the strain did

1 not grow at the breakpoint concentration of penicillin G, the strain was defined as  
2 penicillin G-susceptible (PS). In contrast, when the strain grew at the breakpoint  
3 concentration, the strain was defined as penicillin G-unsusceptible (PU). The MIC  
4 values and the susceptibility rates of PS strains against antibiotics were compared  
5 with those of PU strains.

6

### 7 **Statistical analysis**

8 Statistical comparisons of the susceptibility rates and incidence of  
9  $\beta$ -lactamase-producing bacteria were performed by  $X^2$  test.

10

## 11 **RESULTS**

### 12 **Bacterial examination**

13 A total of 664 strains were isolated from the test cases. Viridans streptococci,  
14 *Peptostreptococcus*, *Gemella*, pigmented and nonpigmented *Prevotella*,  
15 *Porphyromonas*, and *Fusobacterium* were predominant (Table I). Fundamentally,  
16 there was no difference in the bacteriologic data as regards the type of infection  
17 (dentoalveolar infections, periodontitis, and pericoronitis) and in presence or absence  
18 of past administration of antibiotics (data not shown). Antimicrobial susceptibilities  
19 were determined in viridans streptococci, *Peptostreptococcus*, pigmented and  
20 nonpigmented *Prevotella*, *Porphyromonas*, and *Fusobacterium*.

21

### 22 **Relation between the isolation flora and type of the infection**

23 Most of the dentoalveolar infections, periodontitis, and pericoronitis were mixed  
24 infections involving a number of bacterial species (Table II). Average numbers of  
25 isolated strains per abscess of dentoalveolar infections, periodontitis, and



1 pericoronitis were 4.1 (range 1-10), 4.3 (range 2-7), and 3.7 (range 2-6), respectively.  
2 Anaerobes were isolated from 90.6% to 100% in the three types of infection. Most  
3 of the facultative anaerobes isolated from the three types of infection were viridans  
4 streptococci. Isolation flora in all three types of infection were similar to one  
5 another, although aerobes and facultative anaerobes were found more frequently in  
6 the dentoalveolar infections than in cases of periodontitis and pericoronitis (Table II).  
7 More than half of each odontogenic infection had mixed flora including both strict  
8 anaerobes and facultative anaerobes; this was especially the case with viridans  
9 streptococci.

#### 11 **Susceptibility to penicillin G**

12 Viridans streptococci showed a susceptibility rate of 77% and 0.25 $\mu$ g/ml of MIC<sub>90</sub>  
13 value to penicillin G, suggesting that penicillin G would work well to eradicate  
14 viridans streptococci (Table III). *Peptostreptococcus*, *Porphyromonas*, and  
15 *Fusobacterium* showed 86%, 100%, and 89% susceptibility rates, respectively, and  
16 their MIC<sub>90</sub> values were low. Although 72% of pigmented and 82% of  
17 nonpigmented *Prevotella* were susceptible to penicillin G, their MIC<sub>90</sub> values were  
18 very high ( $\geq 16\mu$ g/ml). Eighty-five percent (22 of 26) of the PU strains of pigmented  
19 *Prevotella* were  $\beta$ -lactamase positive, whereas 0% (0 of 67) of the PS strains were  
20  $\beta$ -lactamase positive; these results were significant ( $P < .0001$ ). In nonpigmented  
21 *Prevotella*, all PU strains produced  $\beta$ -lactamase, but none of the PS strains produced  
22 it ( $P < .0001$ ).

#### 24 **Correlation of the susceptibility to penicillin G with that to the other antibiotics**

25 Cefazolin worked well against viridans streptococci, *Peptostreptococcus*,

1 *Porphyromonas*, and *Fusobacterium* (Table IV). However, PU strains of pigmented  
2 and nonpigmented *Prevotella* showed greater MIC<sub>50</sub> and MIC<sub>90</sub> values, and  
3 significantly smaller susceptibility rates than did the PS strains ( $P < .0001$ )(Table IV).  
4 All cefazolin-unsusceptible strains (MIC,  $\geq 16\mu\text{g/ml}$ ) of pigmented and nonpigmented  
5 *Prevotella* produced  $\beta$ -lactamase. Cefmetazole was also effective against viridans  
6 streptococci, *Peptostreptococcus*, *Porphyromonas*, and *Fusobacterium* (Table V).  
7 Moreover, cefmetazole worked well against both PS and PU strains of pigmented and  
8 nonpigmented *Prevotella* (Table V).

9 Only 55% of the PS viridans streptococci were susceptible to erythromycin.  
10 Surprisingly, PU viridans streptococci was not susceptible to erythromycin at all, and  
11 this susceptibility rate was significantly lower than that of the PS strains  
12 ( $P < .0005$ )(Table VI). The MIC<sub>50</sub> and MIC<sub>90</sub> values of PS and PU strains of  
13 *Fusobacterium* were very high. Erythromycin was effective against only 29% and  
14 0% of PS and PU *Fusobacterium*, respectively.

15 In viridans streptococci, clindamycin was effective against 54% of the PS strains  
16 and 0% of the PU strains, respectively (Table VII). However, the MIC<sub>90</sub> values of  
17 clindamycin against both strains were the same, namely,  $0.5\mu\text{g/ml}$ . Clindamycin  
18 showed a quite strong antimicrobial activity against all strict anaerobes tested. In  
19 particular, clindamycin worked very well against pigmented and nonpigmented  
20 *Prevotella*, regardless of their susceptibilities to penicillin G (Table VII).

21 Although the antimicrobial activity of minocycline against the PU strains of  
22 pigmented *Prevotella* was decreased, minocycline was effective against most of the  
23 bacteria tested (Table VIII).

24 Only 56% of PS viridans streptococci were susceptible to levofloxacin (Table IX),  
25 and the PU viridans streptococci showed significantly smaller susceptible rate (25%)

1 than PS strains ( $P < .005$ ). Levofloxacin was effective against strict anaerobes,  
2 although its antimicrobial activity against *Fusobacterium* was weaker than when in  
3 contact with other bacteria.

## 4 5 **DISCUSSION**

6 Many investigators have demonstrated that viridans streptococci,  
7 *Peptostreptococcus*, *Prevotella*, *Porphyromonas*, and *Fusobacterium* are frequently  
8 isolated from orofacial odontogenic infections.<sup>1-6,15,16</sup> Our bacteriologic data was in  
9 good agreement with that of these previous studies. The present study was analyzed  
10 with respect to isolation flora and type of infection. Most of patients had mixed  
11 infections, regardless of the type of infection that had initially been diagnosed (Table  
12 II). The average number of isolates per abscess was approximately four strains,  
13 which was a finding in agreement with those of other reports.<sup>15,16</sup> Only small  
14 differences in the isolated flora were observed among these types of infections (Table  
15 II). Strict anaerobes were found in almost of all of the patients, and these were often  
16 accompanied with facultative anaerobes, especially streptococci, regardless of the  
17 type of infection. It has been reported that a combination of anaerobic gram-positive  
18 cocci and anaerobic gram-negative rods were found frequently in dental root canal  
19 infections.<sup>17,18</sup> In the present study, the combination of strict anaerobic  
20 gram-positive cocci and strict anaerobic gram-negative rods was also found somewhat  
21 frequently in all types of infection examined. The present study suggests that the  
22 combination may be associated with all kinds of odontogenic infections. Further  
23 study of individual pathogens in various bacterial combinations is required to  
24 elucidate the role of these pathogens in the occurrence and prognosis of odontogenic  
25 infection.

1 Determination of the respective breakpoints may be important to analyze  
2 susceptibility data and to estimate antimicrobial effectiveness.<sup>7-9</sup> In general,  
3 breakpoints are determined based on data concerning the clinical outcome, the  
4 pharmacology of the agents, e.g., tissue and serum concentrations, degree of  
5 protein-binding, distribution of susceptibility of bacteria to agents, etc.<sup>7</sup> However,  
6 the specific breakpoints against pathogens in odontogenic infections have not been  
7 established. When antibiotics are administered, concentrations of antibiotics in oral  
8 and maxillofacial regions are much smaller than those found in serum samples.<sup>19-21</sup>  
9 In addition, the respective concentrations of antibiotic vary according to oral and  
10 maxillofacial regions; concentrations at the mandibular bone are lower than those in  
11 the dental alveolar serum, dental follicle, and gingiva.<sup>19-21</sup> Thus, it may be difficult  
12 to determine the special breakpoints for orofacial odontogenic infections. In the  
13 present study, the susceptibility breakpoints were determined by NCCLS criteria,<sup>7-9</sup>  
14 which are widely used in various bacterial studies. However, NCCLS breakpoints  
15 might be too strict for some of test antibiotics because the breakpoints are below the  
16 typical serum or tissue concentrations of the antibiotics. The bacterial strains that  
17 were determined to be unsusceptible to certain antibiotics according to the present  
18 criteria might actually be clinically susceptible to those antibiotics, as they may be  
19 affected by other factors, such as infection site or dosage.

20 The effectiveness of penicillins against viridans streptococci and  
21  $\beta$ -lactamase-producing anaerobic gram-negative rods has been previously debated in  
22 the literatures.<sup>1-6,22</sup> In the present study, the growth of 90% of viridans streptococci  
23 was inhibited at 0.25 $\mu$ g/ml penicillin G despite a susceptibility rate of 77% (Table III),  
24 indicating that penicillins remain reasonably effective against viridans streptococci.  
25 Seventy-two percent and 82% of pigmented and nonpigmented *Prevotella* were

1 susceptible to penicillin G at the tested concentrations, respectively, and their MIC<sub>90</sub>  
2 values were high ( $\geq 16\mu\text{g/ml}$ ). Notably, PU strains of pigmented and nonpigmented  
3 *Prevotella* were shown to produce  $\beta$ -lactamase more frequently than did PS strains  
4 ( $P < .0001$ ), indicating that the resistance of *Prevotella* against penicillin G is  
5 correlated with  $\beta$ -lactamase production. It is important that, despite this resistance,  
6 more than 70% of pigmented and nonpigmented *Prevotella* were susceptible to  
7 penicillin G at the tested concentrations.

8 Cephalosporins should generally not be prescribed for patients who have immediate  
9 hypersensitivity reactions to penicillin, because some of these patients may also be  
10 allergic to several other  $\beta$ -lactam antibiotics.<sup>23</sup> On the other hand, the  
11 cephalosporins are bactericidal and have few side effects; some of them have broader  
12 antimicrobial spectra and show stronger bactericidal activity against the pathogens  
13 specific to orofacial odontogenic infections.<sup>23</sup> In the present study, cefazolin and  
14 cefmetazole were shown to exert a great antimicrobial activity against the viridans  
15 streptococci, *Peptostreptococcus*, *Porphyromonas*, and *Fusobacterium* (Tables IV and  
16 V). Interestingly, the PU strains of pigmented and nonpigmented *Prevotella*,  
17 compared with the PS strains, were more resistant to cefazolin ( $P < .0001$ ). In  
18 contrast, cefmetazole was active against all test bacteria. Cefazolin belongs to the  
19 first-generation cephalosporins, and is vulnerable to  $\beta$ -lactamase,<sup>23</sup> while the stability  
20 of cefmetazole in response to  $\beta$ -lactamase has been confirmed.<sup>23,24</sup>  
21  $\beta$ -Lactamase-stable cephalosporins, including cefmetazole, are effective against  
22 infections. However, these antibiotics are expensive.<sup>6</sup> In addition, some of these  
23 cephalosporins, including cefmetazole, are intravenously administered antibiotics.<sup>23</sup>  
24 The high cost or the inconvenience of intravenous administration of antibiotics may  
25 preclude wide use against odontogenic infections.

1 Erythromycin and clindamycin have been prescribed to patients who are allergic to  
2 penicillin.<sup>1-6</sup> However, it has been noted that erythromycin is not effective against  
3 *Fusobacterium*.<sup>5,25</sup> Our findings confirmed the poor antimicrobial activity of  
4 erythromycin against *Fusobacterium* (Table VI). Furthermore, erythromycin was not  
5 effective against viridans streptococci. In particular, erythromycin showed only  
6 weak antimicrobial activity against the PU strains. It has been demonstrated that  
7 *Streptococcus* and *Fusobacterium* are more frequently isolated from severe  
8 odontogenic infections than from milder infections.<sup>26</sup> The results of the present  
9 study suggest that erythromycin may be effective against mild or moderate infections  
10 in people with penicillin allergies, but it may not be suitable in cases of more severe  
11 infection. In addition, even in cases in which penicillin therapy fails, erythromycin  
12 may not be recommended.

13 Clindamycin is a powerful antibiotic against strict anaerobes including  
14  $\beta$ -lactamase-producing bacteria.<sup>1-5,27</sup> Our findings confirmed that clindamycin is a  
15 powerful agent against strict anaerobes, particularly against pigmented and  
16 nonpigmented *Prevotella* (Table VII). In the present study, the susceptibility rates of  
17 viridans streptococci to clindamycin, according to the breakpoint determined by  
18 NCCLS,<sup>7</sup> were low. However, growth of most viridans streptococci (both the PS and  
19 the PU strains) was inhibited by 0.5 $\mu$ g/ml clindamycin. Clindamycin produces high  
20 alveolar concentrations,<sup>3</sup> and bactericidal activity is achieved clinically with the usual  
21 recommended dose.<sup>2</sup> In addition, clindamycin might increase host defence  
22 potential,<sup>28-30</sup> and inhibit  $\beta$ -lactamase production.<sup>31</sup> Thus, clindamycin would be  
23 effective in the treatment of infections. However, because of its propensity to cause  
24 antibiotic-associated colitis, it has not been widely used in more routine cases of mild  
25 to moderate infections.<sup>1,3</sup> We recommend clindamycin for the treatment of severe

1 infections, or in cases in which penicillin therapy has failed.

2 Many studies have indicated widespread resistance to tetracyclines.<sup>1,3</sup> In the  
3 present study, although the antimicrobial activity against the PU pigmented *Prevotella*  
4 was slightly decreased, minocycline was effective against all test bacteria (Table VIII).  
5 Although minocycline is bacteriostatic, it exerts greater antimicrobial activity against  
6 strict anaerobic bacteria than that of tetracycline or other parent compounds.<sup>3,32</sup> In  
7 cases in which infection is mild or moderate, minocycline may be effective, especially  
8 for patients allergic to penicillin or in cases of penicillin therapy failure. However,  
9 when minocycline is prescribed, an attention should be paid to its adverse effects, e.g.,  
10 gastrointestinal upset, photosensitivity, tooth discoloration.<sup>2,3</sup>

11 The present study demonstrated that less than 60% of viridans streptococci were  
12 susceptible to levofloxacin (Table IX), a fluoroquinolone, which was not as effective  
13 against strict anaerobic bacteria as the other test antibiotics. In addition,  
14 fluoroquinolones are less cost-effective than the other antibiotics. Thus, the present  
15 results do not suggest that fluoroquinolones be used for the treatment of such  
16 infections.

17 In conclusion, viridans streptococci, anaerobic gram-positive cocci, and anaerobic  
18 gram-negative rods were isolated frequently from orofacial odontogenic infections.  
19 Mixed infection of strict anaerobes with facultative anaerobes, especially viridans  
20 streptococci, was predominant in odontogenic infections regardless of the type of  
21 infection. When orofacial odontogenic infections are treated with antibiotics, an  
22 antimicrobial spectrum against both viridans streptococci and oral strict anaerobes  
23 may be required. Penicillin still possesses powerful antimicrobial activity against  
24 major pathogens in orofacial odontogenic infections. However,  
25  $\beta$ -lactamase-producing bacteria may be resistant to penicillin. The susceptibility

1 results suggest that cefazolin may not have more advantages than penicillin, but  
2 cefmetazole may be more effective against infection than penicillin because  
3 cefmetazole possesses strong antimicrobial activity against  $\beta$ -lactamase-producing  
4 bacteria. Moreover, clindamycin may be effective in the treatment of orofacial  
5 odontogenic infections. Minocycline also demonstrated good antimicrobial activity.  
6 However, the findings of the present study indicate that erythromycin and  
7 levofloxacin are of questionable benefit in the treatment of severe orofacial  
8 odontogenic infections.

9

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**Table I.** Organisms isolated from orofacial odontogenic infections

<i>Aerobes</i>	<i>Number of isolates</i>	<i>Anaerobes</i>	<i>Number of isolates</i>
Viridans streptococci	139	<i>Peptostreptococcus</i>	105
<i>Staphylococcus</i>	9	Pigmented <i>Prevotella</i>	93
<i>Corynebacterium</i>	9	<i>Fusobacterium</i>	90
<i>Campylobacter</i>	9	Nonpigmented <i>Prevotella</i>	56
<i>Neisseria</i>	8	<i>Gemella</i>	36
<i>Actinomyces</i>	7	<i>Porphyromonas</i>	35
<i>Lactobacillus</i>	6	<i>Bacteroides</i>	14
<i>Enterobacter</i>	3	<i>Eubacterium</i>	9
<i>Haemophilus</i>	3	<i>Veillonella</i>	8
<i>Pseudomonas</i>	2	<i>Propionibacterium</i>	2
<i>Micrococcus</i>	1	Unidentified anaerobic gram-positive coccus	1
<i>Enterococcus</i>	1	Unidentified anaerobic gram-positive rods	6
<i>Klebsiella</i>	1	Unidentified anaerobic gram-negative rods	9
<i>Branhamella</i>	1		
Unidentified aerobic gram-negative rods	1		
Total	200	Total	464

**Table II.** Relation between the isolated flora and type of odontogenic infections.

<i>Isolated flora</i>	<i>Number of cases (Proportion, %)</i>		
	<i>Dentoalveolar Infection (n=128)</i>	<i>Periodontitis (n=24)</i>	<i>Pericoronitis (n=11)</i>
Single bacterial species			
Strict anaerobe	2 (1.6)	0	0
Facultative anaerobe	4 (3.1)	0	0
Aerobe	0	0	0
Plural bacterial species			
Strict anaerobes alone	31 (24.2)	5 (20.8)	3 (27.3)
AGPC & AGNR *	24(18.8)	3(12.5)	3(27.3)
AGNR *	3 (2.3)	1 (4.2)	0
AGPC *	4 (3.1)	1 (4.2)	0
Strict anaerobes & Facultative anaerobes	75 (58.6)	16 (66.7)	6 (54.5)
AGPC & AGNR & Facultative anaerobes *	41(32.0)	8(33.3)	4(36.4)
AGNR & Facultative anaerobes	24(18.8)	4(16.7)	1 (9.1)
AGPC & Facultative anaerobes	5 (3.9)	3(12.5)	1 (9.1)
AO & Facultative anaerobes	5 (3.9)	1 (4.2)	0
Strict anaerobes & Aerobes	1 (0.8)	0	1 (9.1)
Strict anaerobes & Facultative anaerobes & Aerobes	7 (5.5)	2 (8.3)	1 (9.1)
Facultative anaerobes alone	5 (3.9)	1 (4.2)	0
Facultative anaerobes & Aerobes	3 (2.3)	0	0
Aerobes alone	0	0	0

AGPC, Strict anaerobic gram-positive cocci; AGNR, Strict anaerobic gram-negative rods; AO, strict anaerobes other than AGPC and AGNR.

\*A few cases contained AO.

# Organisms isolated from orofacial odontogenic infections

<i>Aerobes</i>	<i>Number of isolates</i>		<i>Anaerobes</i>	<i>Number of isolates</i>	
	<i>Antibiotics (-)*</i> (72 cases)	<i>Antibiotics (+)†</i> (91 cases)		<i>Antibiotics (-)*</i> (72 cases)	<i>Antibiotics (+) †</i> (91 cases)
Viridans streptococci	69	70	<i>Peptostreptococcus</i>	43	62
<i>Staphylococcus</i>	3	6	<i>Gemella</i>	16	20
<i>Micrococcus</i>	0	1	<i>Eubacterium</i>	7	2
<i>Enterococcus</i>	0	1	<i>Propionibacterium</i>	1	1
<i>Corynebacterium</i>	7	2	Pigmented <i>Prevotella</i>	32	60
<i>Lactobacillus</i>	3	3	Nonpigmented <i>Prevotella</i>	23	32
<i>Actinomyces</i>	4	3	<i>Porphyromonas</i>	18	16
<i>Neisseria</i>	3	5	<i>Fusobacterium</i>	38	50
<i>Pseudomonas</i>	0	2	<i>Bacteroides</i>	3	10
<i>Enterobacter</i>	0	3	<i>Veillonella</i>	3	5
<i>Klebsiella</i>	0	1	Unidentified anaerobic gram-positive coccus	0	1
<i>Branhamella</i>	0	1	Unidentified anaerobic gram-positive bacilli	4	1
<i>Heamophilus</i>	2	1	Unidentified anaerobic gram-negative bacilli	3	6
<i>Campylobacter</i>	4	5			
Unidentified aerobic gram-negative bacillus	1	0			
Average number of isolates	1.3	1.1		2.7	2.9

\* Patients who had not received any antibiotics before specimen collection.

† Patients who had received antibiotics before specimen collection.

**Table III.** Antimicrobial susceptibility to penicillin G

<i>Pathogen</i>	<i>MIC</i> ( $\mu\text{g/ml}$ )*			<i>Susceptibility rate</i> (%)†
	<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	$\leq 0.015 - 0.5$	0.12	0.25	77
<i>Peptostreptococcus</i>	$\leq 0.015 - 4$	$\leq 0.015$	2	86
Pigmented <i>Prevotella</i>	$\leq 0.015 - 64$	$\leq 0.015$	32	72
Nonpigmented <i>Prevotella</i>	$\leq 0.015 - 64$	$\leq 0.015$	16	82
<i>Porphyromonas</i>	$\leq 0.015 - 0.5$	0.03	0.12	100
<i>Fusobacterium</i>	$\leq 0.015 - 2$	0.03	1	89

\*50% and 90%, MIC<sub>50</sub> and MIC<sub>90</sub>, respectively.

†The breakpoints of penicillin G against viridans streptococci and anaerobes are 0.12  $\mu\text{g/ml}$  and 0.5  $\mu\text{g/ml}$ , respectively.



**Table IV.** Antimicrobial susceptibility to cefazolin

<i>Pathogen</i>	<i>Type of strain*</i>	<i>Number of strain</i>	<i>MIC(μg/ml) †</i>			<i>Susceptibility rate (%)‡</i>
			<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	PS	107	≤0.015 - 4	0.25	2	100
	PU	32	2 - 4	2	4	100
<i>Peptostreptococcus</i>	PS	90	≤0.015 - 2	0.06	1	100
	PU	15	≤0.015 - 8	0.03	8	100
Pigmented <i>Prevotella</i>	PS	67	≤0.015 - 0.5	0.03	0.12	100
	PU	26	≤0.015 - 64	2	32	73 §
Nonpigmented <i>Prevotella</i>	PS	46	≤0.015 - 4	0.06	1	100
	PU	10	4 - 64	16	64	30 §
<i>Porphyromonas</i>	PS	35	≤0.015 - 2	0.25	2	100
<i>Fusobacterium</i>	PS	80	≤0.015 - 8	0.12	1	100
	PU	10	0.06 - 0.5	0.06	0.06	100

\* PS, penicillin G susceptible-strains; PU, penicillin G unsusceptible-strains.

All test *Porphyromonas* strains were susceptible to penicillin G.

† 50% and 90% indicate MIC<sub>50</sub> and MIC<sub>90</sub>, respectively.

‡ The breakpoints of cefazolin against viridans streptococci and anaerobes are 8 μg/ml.

§  $P < .0001$ . Statistically significant difference from that of PS strains.

**Table V.** Antimicrobial susceptibility to cefmetazole

<i>Pathogen</i>	<i>Type of strain*</i>	<i>Number of strain</i>	<i>MIC(<math>\mu\text{g/ml}</math>) †</i>			<i>Susceptibility rate (%)‡</i>
			<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	PS	107	$\leq 0.015 - 8$	1	8	100
	PU	32	4 - 8	8	8	100
<i>Peptostreptococcus</i>	PS	90	$\leq 0.015 - 4$	0.12	1	100
	PU	15	$\leq 0.015 - 16$	0.25	16	100
Pigmented <i>Prevotella</i>	PS	67	$\leq 0.015 - 0.5$	$\leq 0.015$	0.5	100
	PU	26	0.03 - 8	0.5	2	100
Nonpigmented <i>Prevotella</i>	PS	46	$\leq 0.015 - 64$	0.06	8	96
	PU	10	0.03 - 8	4	4	100
<i>Porphyromonas</i>	PS	35	$\leq 0.015 - 1$	0.12	0.25	100
<i>Fusobacterium</i>	PS	80	$\leq 0.015 - 16$	0.5	4	100
	PU	10	0.5 - 8	0.5	8	100

\*, † See Table IV.

‡ The breakpoints of cefmetazole against viridans streptococci and anaerobes are 8  $\mu\text{g/ml}$  and 16  $\mu\text{g/ml}$ , respectively.

**Table VI.** Antimicrobial susceptibility to erythromycin

<i>Pathogen</i>	<i>Type of strain*</i>	<i>Number of strain</i>	<i>MIC(μg/ml) †</i>			<i>Susceptibility rate (%)‡</i>
			<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	PS	107	≤0.015 - 8	0.25	1	55
	PU	32	0.5 - 64	0.5	2	0 §
<i>Peptostreptococcus</i>	PS	90	≤0.015 - 64	1	8	89
	PU	15	≤0.015 - 64	0.5	64	80
Pigmented <i>Prevotella</i>	PS	67	≤0.015 - 1	0.12	1	100
	PU	26	0.06 - 64	0.5	32	77 §
Nonpigmented <i>Prevotella</i>	PS	46	≤0.015 - 64	0.5	32	89
	PU	10	0.03 - 64	0.06	32	80
<i>Porphyromonas</i>	PS	35	≤0.015 - 64	≤0.015	0.25	94
<i>Fusobacterium</i>	PS	80	0.03 - 64	8	64	29
	PU	10	8 - 64	8	64	0

\*,† See Table IV.

‡ The breakpoints of erythromycin against viridans streptococci and anaerobes are 0.25 μg/ml and 4 μg/ml, respectively.

§  $P < .0005$ . Statistically significant difference from that of PS strains.

**Table VII.** Antimicrobial susceptibility to clindamycin

<i>Pathogen</i>	<i>Type of strain*</i>	<i>Number of strain</i>	<i>MIC(<math>\mu\text{g/ml}</math>) †</i>			<i>Susceptibility rate (%)‡</i>
			<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	PS	107	$\leq 0.015 - 1$	0.25	0.5	54
	PU	32	0.5 - 8	0.5	0.5	0 §
<i>Peptostreptococcus</i>	PS	90	$\leq 0.015 - 1$	0.12	0.5	100
	PU	15	$\leq 0.015 - 2$	0.03	2	100
Pigmented <i>Prevotella</i>	PS	67	$\leq 0.015 - 0.03$	$\leq 0.015$	$\leq 0.015$	100
	PU	26	$\leq 0.015 - 0.12$	0.03	0.06	100
Nonpigmented <i>Prevotella</i>	PS	46	$\leq 0.015 - 2$	$\leq 0.015$	0.25	100
	PU	10	$\leq 0.015 - 0.12$	$\leq 0.015$	0.06	100
<i>Porphyromonas</i>	PS	35	$\leq 0.015 - 0.06$	$\leq 0.015$	0.03	100
<i>Fusobacterium</i>	PS	80	$\leq 0.015 - 0.25$	0.06	0.12	100
	PU	10	0.06 - 0.12	0.12	0.12	100

\*,† See Table IV.

‡ The breakpoints of clindamycin against viridans streptococci and anaerobes are 0.25  $\mu\text{g/ml}$  and 2  $\mu\text{g/ml}$ , respectively.

§  $P < .0001$ . Statistically significant difference from that of PS strains.

**Table VIII.** Antimicrobial susceptibility to minocycline

<i>Pathogen</i>	<i>Type of strain*</i>	<i>Number of strain</i>	<i>MIC(<math>\mu\text{g/ml}</math>) †</i>			<i>Susceptibility rate (%)‡</i>
			<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	PS	107	$\leq 0.015 - 2$	0.25	0.5	100
	PU	32	$\leq 0.015 - 64$	0.5	2	94
<i>Peptostreptococcus</i>	PS	90	$\leq 0.015 - 4$	0.12	2	100
	PU	15	$\leq 0.015 - 4$	0.06	4	100
Pigmented <i>Prevotella</i>	PS	67	$\leq 0.015 - 8$	0.03	0.12	94
	PU	26	0.12 - 16	2	8	81
Nonpigmented <i>Prevotella</i>	PS	46	$\leq 0.015 - 2$	0.03	0.5	100
	PU	10	0.03 - 2	0.03	2	100
<i>Porphyromonas</i>	PS	35	$\leq 0.015 - 8$	$\leq 0.015$	2	97
<i>Fusobacterium</i>	PS	80	$\leq 0.015 - 4$	0.06	1	100
	PU	10	0.03 - 2	0.03	2	100

\*,† See Table IV.

‡The breakpoints of minocycline against viridans streptococci and anaerobes are 2  $\mu\text{g/ml}$  and 4  $\mu\text{g/ml}$ , respectively.

**Table IX.** Antimicrobial susceptibility to levofloxacin

<i>Pathogen</i>	<i>Type of strain*</i>	<i>Number of strain</i>	<i>MIC(μg/ml) †</i>			<i>Susceptibility rate (%)‡</i>
			<i>Range</i>	<i>50%</i>	<i>90%</i>	
Viridans streptococci	PS	107	≤0.015 - 64	2	8	56
	PU	32	1 - 16	4	8	25 §
<i>Peptostreptococcus</i>	PS	90	≤0.015 - 8	0.5	1	99
	PU	15	≤0.015 - 8	0.06	8	87
Pigmented <i>Prevotella</i>	PS	67	≤0.015 - 8	0.25	4	90
	PU	26	0.25 - 32	1	4	77
Nonpigmented <i>Prevotella</i>	PS	46	≤0.015 - 32	0.5	1	91
	PU	10	0.25 - 32	2	4	80
<i>Porphyromonas</i>	PS	35	≤0.015 - 16	0.25	1	91
<i>Fusobacterium</i>	PS	80	≤0.015 - 4	1	4	76
	PU	10	0.5 - 4	0.5	4	70

\*,† See Table IV.

‡ The breakpoints of levofloxacin against viridans streptococci and anaerobes are 2 μg/ml.

§  $P < .005$ . Statistically significant difference from that of PS strains.