**TURKISH REPUBLIC
MARMARA UNIVERSITY
INSTITUTE OF HEALTH SCIENCES**

INVESTIGATION OF BACTEREMIA AFTER TOOTHBRUSHING IN ORTHODONTIC PATIENTS

**EMAD AHMAD HUSSEIN
MASTER THESIS**

DEPARTMENT OF ORTHODONTICS

**SUPERVISOR
PROFESSOR DR. NEJAT ERVERDI**

ISTANBUL - 2004

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1. ACKNOWLEDGEMENT

Most of my thanks go to God, for the wisdom and perseverance that he has been bestowed upon me during my work on this thesis, and indeed, through out my life.

I would like to express my thanks to Professor. Dr. Nejat Erverdi the head of the department and my supervisor for his advice, encouragement, assistance, help, and valuable guidance over the period of my study.

I would further like to thank Associate Prof. Dr. Ahu Acar for her patience and persistence in helping me with this thesis. Her consistent advice and encouragement is highly appreciated.

I would also like to thank all other faculty members. Prof. Dr. Nazan Kucukkeles, Associate Prof. Dr. Sibel Biren, Assistant Professor Dr. Toros Alcan, Assistant Prof. Dr. Arzu Demirkaya, and Assistant Professor Dr. Banu Cakirer. My thanks also to Associate Professor Dr. Tanju Kadir in the Department of Microbiology for his contribution to this study.

Very special thanks go to my wife and parents, for their endless patience and continuous support, for being a source of encouragement and inspiration to me through out my life. I am also grateful to all my sisters and brothers for their overwhelming support and encouragement.

Finally, I would like to thank all my friends for being a great help to me and for their continual support.

INVESTIGATION OF BACTEREMIA AFTER TOOTHBRUSHING IN ORTHODONTIC PATIENTS

2. SUMMARY

2.1. English Summary

The aim of this study was to investigate occurrence of bacteremia after toothbrushing in orthodontic patients after using 0.2% chlorhexidine gluconate mouthwash, popular toothpaste, and antimicrobial toothpaste.

This clinical study included 40 healthy adult patients (13 females and 27 males with a mean age of 21.5 years) who were selected from the clinical intake of the orthodontic department in the dental faculty of Marmara University; these patients had not taken antibiotics or had a history of cold in the previous 30 days and they presented good oral hygiene.

This study was carried out in 4 groups; each group was comprised of 10 patients, wearing fixed orthodontic appliances both on the upper and lower teeth. The first group was considered the control group; bacteremia was measured after toothbrushing without any tooth paste. In the second group, 0.2% chlorhexidine gluconate mouth rinse was used before brushing with no tooth paste. In the third group, subjects used a commonly used tooth paste in Turkey. The fourth group used an antimicrobial tooth paste.

In the 4 groups pre- and post- brushing blood samples were obtained using a strict aseptic technique, the post-brushing blood samples were taken within 2 minutes after brushing.

The pre- and post-toothbrushing blood samples from the four groups were microbiologically evaluated using blood culture bottles.

All samples taken before brushing were negative for bacteria. In the control group, after brushing bacteremia was detected in 20% of the group. In the second

group, where 0.2% chlorhexidine was used as a mouthwash, no bacteremia was detected after brushing.

Where bacteremia after brushing was not detected in the antimicrobial toothpaste group, in the normal toothpaste group bacteremia was detected in a prevalence of 20% after brushing.

In conclusion, the application of 0.2% chlorhexidine mouth wash and the use of antimicrobial toothpaste resulted in a decrease in the prevalence of bacteremia after toothbrushing in orthodontic patients but the decrease was not statistically significant. Toothbrushing with conventional tooth paste had the same effect as brushing with no toothpaste on the prevalence of bacteremia.

2.2. Türkçe Özet:

Bu çalışmanın amacı hastaların dişlerini macunsuz fırçaladıktan sonra, %0.2 klorheksidin glukonat ile ağızlarını çalkalayıp fırçaladıktan sonra, antimikrobial diş macunu ve normal diş macunu ile fırçalama sonrası oluşan bakteriyemi oluşumunun incelenmesidir.

Çalışmamıza Marmara Üniversitesi Diş hekimliği Fakültesi Ortodonti Anabilim dalında tedavi görmekte olan 40 sağlıklı yetişkin birey(13 kadın, 27 erkek yaş ortalaması: 21.5) dahil edilmiştir. Bu hastaların hiçbiri son 30 gün içerisinde antibiyotik kullanmamış ve soğuk algınlığı geçirmemişlerdir.

Çalışma 4 gruptan oluşmakta ve her grupta alt ve üst dişlerinde sabit braketler takılan 10 hasta bulunmaktadır. İlk grup kontrol grubu olarak seçilmiş ve bu grup dişlerini sadece fırça ile, macun kullanmadan fırçalamıştır. İkinci grup ağızını %0.2 klorheksidin glukonat ile çalkaladıktan sonra macun kullanmadan fırçalamıştır. Üçüncü grup Türkiye’de yaygın olarak kullanılan bir diş macunu ile dişlerini fırçalamış ve dördüncü grupta antimikrobial diş macunu kullanılmıştır.

Dördüncü. grupta fırçalama öncesi ve 2 dakika sonrasında aseptik teknikle kan örnekleri alınmıştır.

Fırçalama öncesi ve sonrası tüm gruplardan alınan kan örnekleri kan kültürü yapılarak mikrobiyolojik açıdan incelenmiştir.

Fırçalamadan önce alınan tüm örneklerde bakteriyemi oluşumu negatif çıkmıştır. Kontrol grubundaki bireylerin %20’sinde fırçalama sonrası bakteriyemi oluşumu saptanmıştır. %0.2 klorheksidin glukonat kullanan ikinci grup hastalarda, fırçalama sonrası bakteriyemi oluşumu gözlenmemiştir.

Üçüncü grupta dişlerini normal macunla fırçalayan hastaların %20 ‘sinde fırçalama sonrası bakteri oluşumu gözlenirken, antimikrobial macun kullanan dördüncü grup hastalarda fırçalama sonrası bakteri oluşumu gözlenmemiştir.

Sonuç olarak, %0.2 klorheksidin glukonat ve antimikrobiyal diş macunu kullanımı, hastalarda fırçalama sonrasında bakteriyemi oluşum riskini

düşürmüş ancak bu düşüş istatistiksel olarak anlamlı bulunmamıştır. Dişleri normal macun ile fırçalama ve macunsuz fırçalama arasında bakteriyemi oluşumu açısından bir fark bulunamamıştır.

3. ABBREVIATIONS

1. *P* : Probability
2. % : Percentage
3. < : Less than
4. > : More than
5. Fig. : Figure
6. et al : And others
7. mL : Milliliter
8. CFU : Colony-forming unit
9. AHA : American Heart Association
10. TBS : Tryptic Broth Soy

4. INTRODUCTION

In the 1930s, it became clear that dental treatment may induce bacteremia, with the potential to produce distant infections such as infective endocarditis. Although the probability of bacteremia associated with dental procedures depends on the invasive procedure performed and the amount of oral inflammation present, but bacteremia was also shown to occur after daily procedures such as toothbrushing, dental flossing, and chewing (50, 57, 71).

The total oral microflora is greater after orthodontic bands are placed on the teeth than before band placement. It is expected that the increase in oral microflora is caused by the increase of areas of plaque retention, and the increase in the number of the oral microorganisms was directly related to the number of bands placed in the mouth. Concluding that orthodontic patients liable to infective endocarditis may have a higher chance to develop bacteremia (9).

Since 1955, antibiotic prophylaxis has been advocated to prevent such metastatic infections. The American Heart Association proposed antibiotic prophylaxis for infectious endocarditis in some orthodontic procedures. The American Heart Association recommended antibiotic prophylaxis in the initial placement of orthodontic bands but not brackets, while endocarditis prophylaxis is not recommended by the AHA for orthodontic appliance adjustment (23).

Antibiotic prophylaxis given prior to dental treatment may prevent bacteremia in some clinical situations, with the caveat that it is impossible to predict which patient will develop bacteremic infection and the risk associated with a particular treatment procedure. Moreover, frequent use of antibiotic prophylaxis makes the treatment more expensive and may trigger adverse reactions, such as hypersensitivity, blood disorders, gastrointestinal problems, bacterial resistance, and interactions with other drugs (36).

As bacteremia is proved to occur with oral hygiene procedures like toothbrushing, and the orthodontic appliances increase the probability of

occurrence of bacteremia, antibiotic prophylaxis cannot be prescribed on daily basis during orthodontic treatment, other methods must be introduced to decrease the total number of oral microorganisms. Antimicrobial tooth pastes and mouth rinse with antiseptic solution such as chlorhexidine 0.2%, may effectively lower the number of bacteria in oral cavity, hopefully, lessening the chances of bacteremia during dental treatment (42, 50, 57, 71).

The aim of our study is to protect the patients who are susceptible to infectious endocarditis during orthodontic treatment, through investigating the incidence of bacteremia after toothbrushing in orthodontic patients using widely used toothpaste and toothbrushing without a toothpaste, compared to antiseptics like 0.2% chlorhexidine gluconate and antimicrobial toothpaste.

5. LITERATURE REVIEW

5.1 Oral Microflora

The mucous membrane of the mouth and pharynx are often sterile at birth but may be contaminated by passage through the birth canal. Within 4-12 hours after birth, streptococci become established as most prominent members of the resident flora and remain so for life. Early in life, aerobic and anaerobic *staphylococci*, gram negative *diplococci* (*neisseriae*, *Moraxella catarrhalis*), *diphtheroids*, and occasional *lactobacilli* are added. In the pharynx the prominent organisms are non-hemolytic and alpha-hemolytic *streptococci* and *neisseriae*, *Staphylococci*, *Haemophilus*, *pneumococci*, *Mycoplasma*, and *Prevotella* are also encountered (62).

After the eruption of teeth, plaque will be formed on tooth surfaces, both supragingival and subgingival. Plaque is generally the non mineralized microbial accumulation that adheres to tooth surfaces and orthodontic and prosthetic appliances. Plaque itself has its microflora, and its composing bacteria were demonstrated to increase in composition after orthodontic appliances been fixed on tooth surfaces. Table 5.1 shows the approximate proportional distribution of bacteria on various oral surfaces, in plaque, and in saliva (11, 40, 41).

Bacteria	Gingival Crevice	Coronal Plaque	Tongue Dorsum	Buccal Mucosa	Saliva
<i>Streptococcus salivarius</i>	<0.5	<0.5	20	11	20
<i>Streptococcus mitis</i>	8	15	8	60	20
<i>Streptococcus sanguis</i>	8	15	4	11	8
<i>Streptococcus mutans</i>	?	0-50	<1	<1	<1
<i>Enterococci</i>	0-10	<0.1	<0.01	<0.1	<0.1
<i>Gram-positive filaments</i>	35	42	20	?	15
<i>Lactobacilli</i>	<1	<0.005	<0.1	<0.1	<1
<i>Veillonella spp.</i>	10	2	12	1	10
<i>Neisseria spp.</i>	<0.5	<0.5	<0.5	0.5	<1
<i>Bacteroides oralis</i>	5	5	4	?	?
<i>Bacteroides melaninogenicus</i>	6	<1	<1	<1	<1
<i>Vibrio sputorum</i>	5	1	<0.5	0.5	?
<i>Spirochetes</i>	2	<0.1	<0.1	<0.1	<0.1
<i>Fusobacterium spp.</i>	3	4	1	?	<1

Table 5.1 Approximate proportional distribution of bacteria on various oral surfaces and in saliva (41)

The significance of the oral microflora is that it can be a source of bacteremia after disruption of capillaries in the gingival tissues. In normal persons, the episodes of bacteremia are brief because of the efficient clearance by the host's immune system. However, in persons with a history of rheumatic heart disease, infective endocarditis, congenital heart defects, prosthetic valve replacement, organic heart murmurs, and aortic valve disease, transient bacteremia increases the risk of infective endocarditis.

Bloom and Brown, using paraffin-stimulated saliva samples, showed that the total oral microflora was greater after orthodontic bands were placed on the teeth than before band placement (9). They concluded that this was caused by the increase of areas for plaque retention and that the increased number of the

organisms was directly related to the number of bands placed in the mouth (Fig. 5.1).

Zachrisson et al showed that even with good cleaning most patients with fixed orthodontic appliances exhibited hyperplastic gingiva and that the orthodontic appliances can act as retention areas for plaque. They saw that this hyperplastic gingiva existed throughout the period of active treatment with a slight increase at subsequent appointments. However, the gingival health was improved within the first month after the bands were removed; they concluded that the gingival changes were transient and that no change to the periodontal tissues was seen (97).

Figure. 5.1 Hyperplastic gingiva in an orthodontic patient

5.2 Bacteremia

In the 1930s, it became clear that dental treatment may induce bacteremia, with potential to produce distant infection such as infective endocarditis (71). Since 1955, antibiotic prophylaxis has been advocated to prevent such metastatic infections. Antibiotic prophylaxis given prior to dental treatment may prevent bacteremia in some clinical situations, with the caveat that it is impossible to predict which patient will develop bacteremic infection and the risk associated with a particular treatment procedure (36). Also, a prolonged incubation period after initial colonization can make it difficult to determine whether an infection results from a specific dental procedure-induced bacteremia or from spontaneous bacteremia associated with daily living.

The probability of bacteremia associated with dental procedures depends on the invasive procedure performed and the amount of oral inflammation present. Table 5.2 shows the incidence of bacteremia with dental treatment and oral hygiene procedures. The proficiency of the microbial isolation method may greatly influence the published incidence rates of bacteremia. A strict anaerobic technique may allow the detection of random spontaneous bacteremia in 60-80% of people at any given time (57).

Dental treatment bacteremia	Oral hygiene bacteremia
Tooth extraction: 51-85%	Toothbrushing: 0-26%
Periodontal surgery: 36-88%	Dental flossing: 20-58%
Scaling and root planning: 8-80%	Toothpicks: 20-40%
Periodontal prophylaxis: 0-40%	Irrigation devices: 7-50%
Endodontics: 0-15%	Chewing: 17-51%

Table 5.2 The incidence of bacteremia with dental treatment and oral hygiene procedures (4, 34, 43, 70)

It is now recognized that the severity of gingival inflammation correlates positively with the incidence and magnitude of bacteremia. Also, infective endocarditis has been detected more frequently in periodontally diseased than periodontally healthy rats. Nevertheless, bacteremia can occur in patients with clinically healthy gingiva (73).

Mostaghim and Millard examined the medical records of 60 patients with bacterial endocarditis at the University of Michigan Hospital from 1962 to 1972 (68). Oral conditions and dental procedures were related to the onset of bacterial endocarditis in 14% of these patients. The dental procedures included prophylaxis, tooth capping, orthodontic treatment, root canal therapy, and extractions. In addition, treatment was given for periocoronitis and dental abscess. The mortality rate for these patients during the 10 years of study was 33% (3, 13, 20, 27, 29, 67).

Although the risks of bacterial endocarditis in patients with a history of rheumatic fever or congenital heart disease were small, patients with a previous episode of bacterial endocarditis or patients with prosthetic heart valves were very susceptible to bacterial endocarditis. Morgan and Bland have shown that, of 119 patients successfully treated for subacute bacterial endocarditis, there was an 8.5% recurrence 6 months to 10 years after the initial episode (67).

Kay stated that transient bacteremia that could result in the development of endocarditis has been known to be caused by a variety of dental procedures, such as extraction of teeth, periodontal surgery, endodontic procedures, brushing of teeth, dental prophylaxis, filling of teeth, and the use of oral irrigation devices. Some of these procedures were more likely to produce a bacteremia than others, and it appeared to be related to the amount of tissue manipulation involved and to the condition of the gingival tissues (50).

In spite of the fact that a variety of dental procedures produce a bacteremia, many patients with a history of rheumatic fever or congenital heart disease were not adequately protected during such procedures. McGowan and Tuohy in a survey of 113 patients with heart lesions in which prophylactic antibiotic therapy would have been appropriate prior to dental treatment, found that 77% of these patients were not given prophylactic antibiotic therapy (65).

5.3.1 Infective Endocarditis

Infective endocarditis is a microbial infection of the endocardial surface usually involving cardiac valves. Prior to the antibiotic era, infective endocarditis was uniformly fatal and was classified as acute, subacute or chronic depending on the rapidity of the development of symptoms and subsequent death. Most endocarditis today would correspond to the old classification of subacute bacterial endocarditis. Infective endocarditis is currently classified according to 1) the offending microorganism (streptococcal, staphylococcal, fungal, etc.), 2) whether the endocarditis affects the original cardiac valve (native valve endocarditis) or a prosthetic replacement valve (prosthetic valve endocarditis) or 3) whether special circumstances have been responsible for the acquisition of the infective endocarditis, including nosocomial (hospital-acquired) endocarditis or intravenous drug abuse (45).

The principal risk factors for infective endocarditis are damage to the endocardium from congenital or rheumatic heart disease, age-induced degeneration of cardiac valves and /or repeated insult from turbulent blood flow, which induces platelet and fibrin deposition (nonbacterial thrombotic vegetation) and subsequent infection via blood-borne bacteria (bacteremia). Contributing factors include the degree and type of valvular damage, frequency and type of bacteremia, microorganism pathogenecity, capability of the microorganism to adhere to the cardiac valves and host defense mechanisms (86). Infective endocarditis may be the result of a single episode of failed host defense during thousands of repeating bacteremic insult over lifetime (75).

5.3.2 Signs and Symptoms of Infective Endocarditis

Early therapeutic intervention with infective endocarditis can greatly reduce morbidity and mortality. Unfortunately, the signs and symptoms of early infective endocarditis can resemble simple influenza.

Initial signs and symptoms are fever, malaise, night chills, anorexia, myalgia and arthralgia. Other less common but important criteria are: back pain, polyarthritis, splenomegaly and anemic pallor. A new or changing cardiac murmur is common.

Other signs and symptoms result from the formation and dissemination of emboli to the brain (cerebral emboli cerebritis and mycotic aneurisms), kidney (infarction and abscess), spleen (infarct), heart (arterial occlusion and myocarditis), and skin (petechiae of the palate, mucosa and conjunctiva). Additional peripheral phenomena include Osler's nodes (small purple, tender nodules in the pulp of fingers and toes), Janeway lesion (small, erythematous maculae on palms and the soles of the feet), and Roth spots (pale-centered oval retinal hemorrhages). Progressive congestive heart failure is an ominous sign (10).

5.3.3 Epidemiology of Infective Endocarditis

The incidence of infective endocarditis ranges from 11 to 50 cases per million population per year (37). A prospective infective endocarditis study from the Netherlands found an incidence rate of 19 per million population (92). The prevalence of infective endocarditis is 1.7 to 4.9 cases per 100 000 person/years in the United States and 2 cases per 100,000 person/years in England and Wales, computed to about 8000-10,000 annual cases in the United States and 1500 annual cases in England and Wales (86, 72).

The incidence of endocarditis has not declined since the advent of antibiotics in 1940s. This might suggest that: 1) antibiotic prophylaxis may be improperly applied (ineffective drug, timing or dose) 2) antibiotic prophylaxis may not be effective, 3) antibiotic prophylaxis may not be directed towards the correct at-risk population, 4) infective endocarditis could be the result of single failed host defense amid repetitive cases of bacteremia (75).

Bacterial endocarditis has a high mortality rate, and successfully treated bacterial endocarditis has a high rate of recurrence (8.5%) of bacterial re-infection and limitation of activity as a result of cardiac decompensation. The 5-year survival rate has been reported at 69% with congestive failure as the principal cause of death (20, 55).

5.3.4 Microbiology of Infective Endocarditis

Streptococcal and staphylococcal strains cause the vast majority of infective endocarditis. The propensity of these organisms to elicit endocarditis is due to at least three factors: 1) their main habitat on skin and mucous membranes, which allows for frequent entry into the blood as random or treatment induced bacteremia, 2) an exceptional ability to adhere to damaged cardiac valves, 3) an

ability to survive and thrive in the nonbacterial thrombotic vegetation of the cardiac valve.

In the era before antibiotics, more than 80% of all endocarditis cases were caused by *streptococci* (the *viridans* group, *enterococci*, *beta-hemolytic* and *Streptococcus pneumoniae*) (89). In 1970s, the incidence of streptococcal endocarditis began to decline to the present 50-60%, with 30-40% of all cases now due to *viridans streptococci* prominent in but not exclusive to the human oral cavity (*S.sanguis*, *Streptococcus mitis*, *Streptococcus anginosus*, *Streptococcus salivarius* and *Streptococcus mutans*). At the New York City Hospital, *S sanguis* and *S mitis* each accounted for 31-47% of all *viridans streptococcal* endocarditis cases for a combined total of 64-87%. *S sanguis* is generally regarded as the single most common causative microorganism for infective endocarditis. About 3% of all infective endocarditis is caused by *S.pneumoniae* and a lesser percent by *beta-hemolytic streptococci* (79).

In a study of 2345 infective endocarditis episodes from 1933-1987 the percentage of each group of organisms was: *streptococci* (56.4%), *staphylococci* (24.9%), gram-negative organisms (5.7%), others (2.7%), fungi (1%) and culture-negative (9.3%) (89).

The decline in streptococcal infective endocarditis probably reflects a rise in the proportion of prosthetic valve patients, intravenous drug abusers, and nosocomial-associated staphylococcus endocarditis and the increase in endocarditis due to HACEK group of organisms: *Haemophilus influenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella kingae* (47).

5.4 Bacteremia in Orthodontic Literature

There are at least 4 reported cases of infective endocarditis reported in the orthodontic literature following orthodontic procedures. Hobson and Clark reported a case of a child that was admitted to the hospital with a two-week history of fever and malaise, the admission was 2 weeks after his last orthodontic appointment during which an archwire was changed and power chain applied for tooth movement. Blood culture grew alpha hemolytic *Streptococcus mitis*, which is sensitive to penicillin and present within the oral microflora (48).

At the Children's Medical Center at Stony Brooks, two children with congenital cardiac defect in whom bacterial endocarditis developed after such adjustments were reported in 1991 by Biancaniello and Romero, in both cases the adjustment of orthodontic appliances was reported 10 days before the onset of the first symptoms (8).

Dajani reported a case with endocarditis caused by ampicillin-resistant *Haemophilus parainfluenzae*, the patient had no previous history of any cardiac abnormality, and she had adjustment of her fixed orthodontic appliance 20 days before the onset of her symptoms, however, the current guidelines of the American Heart Association on the prevention of bacterial endocarditis still do not include a recommendation for antibacterial prophylaxis for "simple adjustment of orthodontic appliances" (24).

A survey concerning the orthodontic management of patients with a history of rheumatic fever or congenital heart disease was carried out by Gaidry and Kudlich to a random sample of 500 orthodontists throughout the United States (39). Two hundred thirty-two surveys were completed and returned. Analysis revealed that 88% of the respondents were aware that they should screen for patients with a history of rheumatic fever or congenital heart disease, only 11% used the antibiotic regimen recommended by the American Heart Association, one half of the respondents thought it was necessary to provide antibiotic coverage during banding, and 38% deemed it necessary for debanding procedures which were

likely to cause some degree of bleeding from the gingival sulcus. Only one half of the respondents would discontinue treatment if a condition of gingivitis developed which did not show signs of improvement, and only 70% provided medication for orthodontic procedures that could result in bacteremia. Furthermore, the results of this survey indicated that there was a great variation in the antibiotic regimen of orthodontic treatment for patients at risk of developing endocarditis and that there was a need to make the orthodontist more aware of the recommendations of the American Heart Association. This survey also revealed that a relatively high percentage of orthodontists do not premedicate patients who are at risk of developing bacterial endocarditis, and it was found that, of those who did premedicate, a great variation existed in their premedication regimens.

In their article, "Management of the orthodontic patient 'at risk' from infective endocarditis", Hobson and Clark assumed that there are no clear guidelines for the application of current antibiotic prophylactic regimes to orthodontic patients at risk from infective endocarditis (49). In order to ascertain current practice, a survey on various aspects of the management of orthodontic patients at risk from infective endocarditis was undertaken. Questionnaires were sent to all 1038 members of the British Society for the Study of Orthodontics and the British Association of Orthodontists. A total of 518 replies were received, 480 (46%) of which were completed in full and analyzed. The results of analysis showed that eight cases of infective endocarditis associated with orthodontic treatment over a 44-year period were reported. The majority of respondents underestimated the number of at risk patients likely to be encountered over a 5-year period. Most orthodontists routinely contact the medical practitioner (62%) or hospital consultant (65%) for advice on the prescription of prophylactic antibiotics. Only 58 (12%) claimed to have refused orthodontic treatment for at risk patients. The majority of respondents advise the use of antibiotic prophylaxis for band placement and removal and manipulation of an unerupted tooth. A high standard of oral hygiene must be established prior to orthodontic treatment for at risk patients. Antibiotic prophylaxis in orthodontics should be used for procedures which cause gingival trauma, for example band

placement and removal. Hobson and Clark recommended daily use of a chlorhexidine mouthwash during treatment and prior to appliance adjustment.

McLaughlin carried out an investigation to assess the incidence of bacteremia after orthodontic banding. Thirty adult volunteers with good oral health, who were not at risk from bacterial endocarditis, were included in this study. An orthodontic band was placed on a first molar of each subject. Venous blood samples were taken before, and 1 to 2 minutes after the molar band was fitted. Microbiologic tests performed on the blood samples revealed a comparatively low incidence of bacteremia (10%) after orthodontic banding (66).

Degling reported in his study that no bacteremia was produced in fully banded orthodontic patients or non banded patients after 5 minutes of chewing bubble gum. Furthermore, no transient bacteremia could be demonstrated after orthodontic banding or debanding (25).

Erverdi et al studied the incidence of bacteremia after orthodontic banding; their study was conducted on 40 healthy orthodontic patients with good oral hygiene. Venous blood samples were obtained with a strict aseptic technique before and after fitting of a molar band in each patient. Microbiologic evaluation of the samples revealed a postoperative bacteremia incidence of 7.5%. The organisms isolated in Erverdi's study were —*S sanguis* and *S mitis*— known to have a strong association with infectious endocarditis (33).

Erverdi et al concluded that, even though a bacteremia incidence of 7.5% after orthodontic banding is considerably lower than the incidences reported in oral hygiene procedures, the orthodontist is advised to evaluate the level of risk of the patient and consider consultation with the patient's cardiologist. They also concluded that the effectiveness of antibacterial mouthwashes in orthodontic banding should be investigated in further studies.

Erverdi et al investigated bacteremia following orthodontic debanding in a study which comprised 30 orthodontic patients with good oral hygiene and upper and lower fixed orthodontic appliances. Blood samples were taken using an aseptic

technique before and after removal of bands and brackets. They found 6.6% bacteremia prevalence in both preoperative and postoperative blood samples (32).

In their third study, Erverdi et al investigated prevalence of bacteremia after orthodontic banding and debanding following 0.2% chlorhexidine gluconate mouthwash application. The banding and debanding groups each composed of 40 patients. In the banding group, patients were asked to rinse their mouth with chlorhexidine gluconate for 60 seconds before fitting the bands. In the debanding group, patients were asked to use the mouthwash immediately before removal of the bands and brackets. In both groups, pre- and post- treatment blood samples were obtained by a strict aseptic technique. In the banding group, no bacteremia was detected in the pretreatment sample, and 2.5% post treatment bacteremia was detected in the post treatment sample. In the debanding group, 2.5% bacteremia was found in both the pre- and post-treatment samples. The prevalence of post treatment bacteremia found in this study was compared to the findings of their previous studies in which the prevalence of bacteremia had been investigated after banding and debanding without a prior application of chlorhexidine mouthwash. They concluded that the application of chlorhexidine mouthwash resulted in a decrease in the prevalence of bacteremia after banding and debanding, but the decrease was not statistically significant (31).

Chung and Kudlick studied the extent of bacteremia experienced by patients undergoing orthodontic treatment with fixed appliances during periods of routine oral hygiene— namely, brushing the teeth. Sixteen orthodontic patients made up the population— 11 who practiced good oral hygiene and five who demonstrated poor oral hygiene. Blood was drawn aseptically from the median cubital vein of the subjects before and 15 minutes after brushing the teeth. An aliquot of each blood specimen was added to separate blood culture bottles and incubated at 37° C for a period of up to 5 days. Blood was also used to determine the immune status of the subjects. Anaerobic bacteria were recovered from the blood of nine of the 16 patients studied; aerobic bacteria were not recovered. A negative blood culture before brushing and positive blood cultures after brushing were expected but did

not occur. Some subjects showed bacteremia before brushing and a negative blood culture after brushing. Others showed bacteremia before and after brushing. The unexpected results could be attributed to the patients eating and/or brushing before starting the test. The study showed the capacity of specific anaerobic bacteria to remain in the bloodstream for a 15-minute period. It also demonstrated a presence of bacteria in the bloodstream before the test began (14).

Schlein, carried out a study to determine whether and to what extent bacteremia occurred after toothbrushing in patients undergoing orthodontic treatment with fixed appliances. Twenty patients were selected, all with negative history of heart or hematologic disorders. These patients had not taken antibiotics or had a history of a cold in the previous 30 days. Blood samples of 20 ml were drawn before and 5 minutes after brushing. The immune status of the patients was tested by measurement of isohemagglutins and immunoglobulin levels. Blood samples were incubated in paired culture bottles containing trypticase soy broth (TSB) with an agar paddle and Columbia broth. All samples taken before brushing were negative for bacteria. Five of the 20 patients (25% of the sample) had positive blood tests after brushing. Both anaerobic and aerobic bacteria were identified from the blood samples. Those patients who were found to have a bacteremia did not display poor oral hygiene (83).

Lucas et al studied the relationship between odontogenic bacteremia and orthodontic treatment procedures. The purpose of their study was to estimate the prevalence and intensity of bacteremia associated with orthodontic treatment procedures. The four procedures investigated were: an upper alginate impression, separator placement, band placement, and adjustment of an arch wire on a fixed appliance. Eighty-one children undergoing general anesthesia (GA) for dento-alveolar surgery related to their orthodontic treatment were randomly allocated to the impression or separator group. A further 61 children, receiving treatment in the Outpatient Department, were included and randomly allocated to the banding or arch wire adjustment groups. A cannula was inserted into either the left or right antecubital fossa using an aseptic technique. A baseline 6 mL sample of blood was

taken before treatment and a second 6 mL sample was taken 30 seconds after the procedure. There was no significant difference in the number of positive blood cultures between baseline (nine, 23 per cent), and following an upper alginate impression (twelve, 31 per cent); between baseline (twelve, 27 per cent), and placement of a separator (fifteen, 36 per cent); between baseline (nine, 36 per cent), and fitting or placement of a band (eleven, 44 per cent); or between baseline (twelve, 33 per cent), and arch wire adjustment (seven, 19.4 per cent). For the separator group only the mean total number of aerobic and anaerobic bacteria combined, isolated from the blood samples (CFU of bacteria per ml of blood), was significantly greater following the placement of a separator (2.2, SD 9.1), compared with baseline (0.9, SD 0.2; $P < 0.02$). This investigation demonstrates that the only orthodontic treatment procedure that causes a significant bacteremia is the placement of a separator (60).

Khurana et al in their article "Orthodontics and infective endocarditis" claimed that infective endocarditis associated with orthodontics is a rare occurrence. And many orthodontic practitioners do not treat patients potentially at risk of developing endocarditis due to the lack of practical guidelines and fear of precipitating the infection. Additionally, they claimed that many patients that undergo orthodontic treatment are inappropriately prescribed antibiotic cover for procedures that have a minimal bacteraemic risk (52).

5.5 Recommendations of The American Heart Association (AHA)

The American Heart Association proposed antibiotic prophylaxis for bacterial endocarditis in some orthodontic procedures. According to the American Heart Association (AHA), endocarditis prophylaxis is recommended in initial placement of orthodontic bands but not brackets, while endocarditis prophylaxis is not recommended for orthodontic appliance adjustment (23).

Although incidence of endocarditis following most procedures in patients with underlying cardiac disease is considerably low, a reasonable approach for endocarditis prophylaxis should consider the following: the degree to which the patient's underlying condition creates a risk of endocarditis; the apparent risk of bacteremia with the procedure (as defined in these recommendations); the potential adverse reactions of the prophylactic antimicrobial agent to be used; and the cost-benefit aspects of the recommended prophylactic regimen. Failure to consider all of these factors may lead to overuse of antimicrobial agents, excessive cost, and risk of adverse drug reactions (23).

The American Heart Association updated its recommendations in 1997 for the prevention of bacterial endocarditis in individuals at risk for this disease. The cardiac conditions which are associated with bacterial endocarditis, the prophylactic regimens and the dental procedures associated with bacterial endocarditis were well explained and listed in tables to ease the role of the dentist (Appendix). We preferred to include recent tables of recommendations by the AHA in this master thesis in order to provide an overall view of this subject (Appendix).

The recent recommendations of the American Heart Association published in 1997, compared to the previous recommendations by Dajani et al carry the following differences: 1) Erythromycin is no more an alternative to Penicillin, 2) 2 grams penicillin instead of 3 grams, 3) the after procedure dose is no more recommended (21).

5.6.1 Additional Measures to Prevent Bacterial Endocarditis

Does antibiotic prophylaxis prevent bacterial endocarditis? Trying to give an answer to this issue, Van der Meer et al conducted a study to assess the efficacy of prophylaxis for bacterial endocarditis on native valves in a nationwide case-control study in the Netherlands. Cases were patients with known cardiac disease in whom endocarditis developed within 180 days of a medical or dental procedure

for which prophylaxis was indicated. Of a total of 438 patients with endocarditis diagnosed during 2 years, 48 were eligible for their study. Controls were patients with the same cardiac status in whom endocarditis did not develop within 180 days of similar procedure; of a total of 889 controls of five hospitals, 200 were eligible. Overall, about 1 in 6 patients in both groups had received prophylaxis. The best estimate of protective efficacy was 4.9 % for first-ever endocarditis occurring within 30 days of a procedure. Endocarditis developed within 30 days of a procedure in only 13% of patients with a previously diagnosed heart lesion which predisposed to the disease. Their findings suggest that strict adherence to generally accepted recommendations for prophylaxis might do little to decrease the total number of patients with endocarditis in the community (93).

Lacassin et al studied the relative risk of infective endocarditis associated with various surgical and dental procedures and the efficacy of antibiotic prophylaxis in France. They concluded that surgical and dental procedures increase the risk of infective endocarditis; from the efficacy rate of antibiotic prophylaxis, they could estimate that the overall incidence of infective endocarditis might be reduced by 5 to 10% by appropriate use of antibiotic prophylaxis in cardiac patients (54).

The medical and dental literature provides abundant information on the ways and means to prevent infective endocarditis. However, nearly all reports designate antibiotics as the central mode prophylaxis and concentrate on infective endocarditis originating from dental care. Recent evidence indicates that prophylactically administered antibiotics have less effect on the incidence of the disease than shifts in the susceptible population (28). Moreover, sizable numbers of bacterial endocarditis are associated with routinely performed activities, such as toothbrushing and mastication, and are not associated with dental treatment per se (17)(71).

There are additional considerations that render the use of antibiotic as the principal vehicle of prevention questionable. Bacterial strains resistant to the administered antibiotics may engender bacterial endocarditis. Moreover, it is

suggested that penicillin-resistant microorganisms are part of the normal flora in at least 7% of the normal population and more in patients who are in frequent contact with antibiotics. Finally, frequent use of antibiotic prophylaxis makes the treatment more expensive and may trigger adverse reactions, such as hypersensitivity, blood disorders, gastrointestinal problems, bacterial resistance, and interactions with other drugs. In fact, several recent publications indicated that bacterial endocarditis developed under the prophylactic regimen recommended by the American Heart Association (90). When one is considering approaches to the prophylaxis of bacterial endocarditis, at least five major elements that play a cardinal role in defining the probabilities of developing bacterial endocarditis must be taken into account. These are 1) patient's history, 2) patient's age, 3) the type of cardiac defect, 4) the type of bacteria, 5) the number of microorganisms that penetrate into the blood-stream. While the first three variables are uncontrollable, some degree of control can be exercised over the later two. The difference in behavior of these two distinct groups of variables must be reflected in the process of medical reasoning. The first group plays a significant role in determining the degree of risk contracting bacterial endocarditis; nevertheless, prevention of bacterial endocarditis can still be enhanced by focusing primarily on the second group.

Mouth rinses with antiseptic solution such as chlorhexidine 0.2%, may effectively lower the number of bacteria in oral cavity, hopefully, lessening the chances of bacteremia during dental treatment.

5.6.2 Antiseptic Mouthwashes

Antiseptic mouthwashes applied immediately prior to dental procedures may reduce the incidence and severity of bacteremia (61). Useful agents may include chloramine-T, povidone-iodine, iodine and glycerin and chlorhexidine. The antiseptic of choice is chlorhexidine applied via gentle oral

rinsing for 1-2 minutes prior to dental treatment. The American Heart Association recommends chlorhexidine irrigation of the gingival sulcus or painting chlorhexidine on isolated dried gingiva for 3-5 minutes before treatment (22). However, Lofthus et al found no difference in the magnitude of bacteremia after scaling or root planning for patients given subgingival irrigation with chlorhexidine, saline or controls (59). Ordinarily, chlorhexidine will be used immediately prior to dental treatment after the systemic antibiotic prophylaxis has reached adequate blood levels, but chlorhexidine alone without systemic prophylaxis in low-risk patients may be appropriate

Sustained or frequent usage of chlorhexidine may not be recommended, as this may result in selection of resistant *streptococci*, *enteric gram-negative rods*, *pseudomona* and *enterococci* (30) (35) (69) (74) (77) (85). These organisms can colonize the oral cavity and induce a type of endocarditis associated with higher mortality rate than the *viridans streptococci* (28).

In addition to the formation of new forms of resistant bacteria, other side effects of the prolonged use of chlorhexidine could be seen like staining of teeth and porcelain, desquamation of gingiva, inflammation of salivary glands ducts and changes in taste.

5.6.3 The Mechanism of Plaque Inhibition By Chlorhexidine

The mechanism of action of a chlorhexidine mouthwash seems to be an immediate and probably short-lived bacteriocidal effect followed by a prolonged bacteriostatic action dependant on antiseptic absorbed by the pellicle coated tooth surface. The marked plaque inhibiting activity shown by chlorhexidine is a unique property demonstrated by the bis-biguanides. Initial elimination of bacteria by the chlorhexidine mouth rinses seem not to be the decisive factor in the plaque inhibition, as antibacterial agents with as high or higher activity against salivary bacteria did not show corresponding clinical effects (80).

Considerable evidence has been accumulated indicating that retention of bis-biguanides in the mouth is the basis for the plaque inhibition. About 30% of the chlorhexidine introduced in the mouth during a mouth rinse is retained. The teeth are not the major retention site, at least not quantitatively, but plaque covered teeth have been shown to bind limited quantities of the drug. Results of studies that used mouth rinses at different pH levels strongly indicate that acidic groups presumably on the macromolecules of the mucus secretions covering the oral surfaces are the receptors responsible for the major share of the retained chlorhexidine. Electrostatic binding between the acidic protein group and the basic bis-biguanide molecules seem to be involved (15).

Chlorhexidine is bound to acidic groups presumably by an electrostatic interaction. Protein extracts from the major salivary glands showed that all the extracts bound the drug at pH's 4.5, and 3.0, but the sublingual gland extracts retained Chlorhexidine below a pH of 3.0. Deviant cations could explain Chlorhexidine from the phosphate and carboxyl groups. It is suggested that a slow displacement of Chlorhexidine from carboxyl binding sites on the oral mucosa by salivary Ca^{++} might explain the long anti-bacterial effect of bis-biguanides in the mouth. Chlorhexidine displaced Calcium from sulfate (16).

Bound sulfate is known to be present in plaque and calculus presumably as a sulfated glycoprotein. A displacement of this kind of the Ca^{++} on which the acidic agglutination factor in plaque are known to be dependant, may be an aspect of plaque-inhibiting activity of Chlorhexidine in vivo.

Chlorhexidine gluconate mouthwash is commercially available in 0.12% and 0.2% concentrations. Similar results have been obtained with the two chlorhexidine concentrations with regards to reduction of plaque accumulation and gingival inflammation.

König et al compared the anti-plaque effect of warm and cold 0.2% chlorhexidine gluconate irrigation on matured human plaque. The antibacterial effect of 47 degrees C "warm" 0.2% chlorhexidine solution was compared with that of 18 degrees C "cold" rinse at the same concentration on newly-formed

supragingival plaque that had been left undisturbed for 72 h. Before and 1 h after a 1-min rinse procedure, plaque was sampled from 10 test persons and vitality determined using vital fluorescence technique. They found out that cold and warm 0.2% chlorhexidine solution reduced plaque vitality significantly from 99.63% to 77.81% ($p=0.014$) and from 98.98% to 51.77% ($p<0.001$), respectively. Rinsing with warm chlorhexidine solution reduced plaque vitality to a significantly greater degree ($p=0.003$) than did cold chlorhexidine. The conclusion of their study was that warm 0.2% chlorhexidine rinse showed a significantly more intensive anti-plaque effect than cold chlorhexidine solution at the same concentration (53).

Beyth et al evaluated the effect of sustained-release chlorhexidine varnish on orthodontic patients. Their study included ten children, ages 10 to 16 years. Bacterial levels of *Streptococcus mutans* and *Actinomyces viscosus* and total counts were evaluated in sputum samples. These counts were evaluated at 4 stages: before orthodontic treatment, at least 2 weeks after bonding of the brackets, 1 week after application of chlorhexidine varnish, and 3 weeks after application of chlorhexidine varnish. Increases in bacterial levels of *S. mutans* and in the total bacterial count were detected after the brackets were bonded. One week after the sustained-release chlorhexidine varnish was applied, a significant decrease of total bacterial levels and *S. mutans* was observed. This decrease persisted for 3 weeks after the first application. No significant change in *A. viscosus* levels occurred during that period. Their results provide additional evidence that sustained-release chlorhexidine varnish decreases *S. mutans* levels in orthodontic patients with fixed appliances and therefore might be useful in preventing caries lesions (7).

5.6.4 Antimicrobial Toothpastes

There is a considerable interest recently, in improving dentifrices by using them as vehicles for chemotherapeutic agents to inhibit plaque, calculus caries and

root hypersensitivity. The pronounced caries preventive-effect of fluorides incorporated in dentifrices has been proved. Substances such as chlorhexidine, penicillin, vaccines, vitamins, dibasic ammonium phosphate, chlorophyll and formaldehyde have proved to be of little therapeutic value in toothpastes (51). Tartar control toothpastes with the active ingredient pyrophosphate are currently available. This ingredient interferes with crystal formation in calculus, and does not affect the fluoride ion in the paste or increase tooth sensitivity. These toothpastes are beneficial only for supragingival calculus they do not affect subgingival calculus formation or gingival inflammation (63). To achieve the greatest effect of anti-calculus toothpaste, the patient's teeth must be cleaned and completely free of supragingival calculus when starting to use the product daily. The inhibitory effect will only work against the deposition of new layers of calculus.

Gaffar et al reviewed several therapeutic approaches and chemical agents that have been used to control dental plaque, plaque microflora and supragingival infections. These include fluoride preparations such as stannous fluoride, oxygenating agents, anti-attachment agents, and cationic and non-cationic antibacterial agents. Among the fluoride preparations, stable stannous fluoride pastes and gels have been shown to reduce supragingival plaque, gingivitis, hypersensitivity and caries. The effect of the oxygenating agents on the supragingival plaque has been equivocal, but recent data indicate that a stable agent that provides sustained active oxygen release is effective in controlling plaque. A polymer, PVPA, which reduced attachment of bacteria to tooth surface was shown to significantly reduce plaque formation in humans. A new generation of antibacterials includes non-ionics such as triclosan, which in combination with a special polymer delivery system, has been shown to reduce plaque, gingivitis, supragingival calculus and dental caries in long-term studies conducted around the world. Unlike the first generation of agents, the triclosan/copolymer/sodium fluoride system is effective in long-term clinical trials and does not cause staining of teeth, increase in calculus, or disturbance in the oral microbial ecology (38).

Dori et al conducted a study which aimed to assess the in vitro

antibacterial effectiveness of three dentifrices containing antimicrobial agents and to test the in vivo anti plaque and anti gingivitis effect of a toothpaste containing triclosan (CAOLA). The in vitro tests showed a marked antibacterial effect of both triclosan and chlorhexidine containing dentifrices. The randomized clinical trial presented good evidences that the triclosan had some but statistically non significant plaque and gingivitis reduction in patients even without previous mechanical cleaning. Nevertheless the triclosan dentifrice was effective in reducing the plaque and gingivitis scores in combination with initial mechanical debridement and oral hygienic instructions (26).

The newly introduced antimicrobial toothpaste The One Drop Only was selected to our study according to its natural constituents. This toothpaste contains according to the information provided by the company etheric oils: clove oil and peppermint oil that are known to have an antimicrobial effect; in addition to the tea tree-oil which is an etheric oil of the Australian tea-tree *Melaleuca alternifolia*, (96).

The essential oil of *Melaleuca alternifolia*, commonly known as tea tree oil, has a long history of use as a topical antiseptic. In recent times it has gained a reputation as a safe, natural and effective antiseptic. This has led to resurgence in popularity and currently it is incorporated as the principal antimicrobial or as a natural preservative in many pharmaceutical and cosmetic products intended for external use (19).

A wide variety of essential oils are known to possess broad-spectrum antimicrobial properties and in many cases this activity is due to the presence of active monoterpene constituents. The chemical composition of tea tree oil has been well defined and consists largely of cyclic monoterpenes of which about 50% are oxygenated and about 50% are hydrocarbons. Several studies have also shown that monoterpenes exert membrane-damaging effects. Examination of *Escherichia coli* cells using electron microscopy after exposure to tea tree oil revealed a loss of cellular electron-dense material and coagulation of cytoplasmic constituents,

although it was apparent that these effects were secondary events that occurred after cell death. Tea tree oil also stimulates leakage of cellular potassium ions and inhibits respiration in *E. coli* cell suspensions, providing evidence of a lethal action related to cytoplasmic membrane damage (19) (64).

Tea tree oil exhibits broad-spectrum antimicrobial activity which can be principally attributed to terpinen-4-ol. The mechanisms of action of tea tree oil and three of its components, 1,8-cineole, terpinen-4-ol, and α -terpineol, against *Staphylococcus aureus* were investigated. Treatment with these agents was found to reduce the viability of *S. aureus* particularly after treatment with 1,8-cineole and α -terpineol. *S. aureus* organisms treated with tea tree oil or its components showed a significant loss of tolerance of *S. aureus* to NaCl. The loss of tolerance to NaCl, and the altered morphology seen by electron microscopy all suggest that tea tree oil and its components compromise the cytoplasmic membrane and cell lysis (12).

Grosso et al compared the antimicrobial activity of tea tree oil, garlic, and chlorhexidine solutions against oral microorganisms. Total microorganisms and mutans streptococci were counted in blood agar and their results showed that chlorhexidine and garlic groups showed antimicrobial activity against mutans streptococci, but not against other oral microorganisms. The tea tree oil group showed antimicrobial activity against mutans streptococci and other oral microorganisms (42).

A pilot study by Arweiler et al to compare the effect of tea tree with the effect of water and chlorhexidine on supragingival plaque found no positive effect on the quality or quantity of supragingival plaque (1).

6. AIM

The aims of this study are

- 1) To investigate occurrence of bacteremia after toothbrushing in orthodontic patients wearing fixed orthodontic appliances, with and without conventional and widely used toothpaste.
- 2) To investigate the effect of rinsing with 0.2% chlorhexidine gluconate prior to toothbrushing on the prevalence of bacteremia in orthodontic patients.
- 3) To investigate the effect of toothbrushing with antimicrobial toothpaste on the prevalence of bacteremia in orthodontic patients.
- 4) To compare the results of the test groups in order to come out with suggestions -according to the results- to decrease the prevalence of bacteremia after toothbrushing on daily basis.
- 5) To come out with a comprehensive study that can provide the clinician with a scientific basis for deciding the treatment of choice for a given patient based on specific criteria.

7. SIGNIFICANCE OF THE STUDY

The present study investigates the incidence of bacteremia after toothbrushing in orthodontic patients with conventional and widely used toothpaste and without a toothpaste, compared to antiseptics like chlorhexidine and antimicrobial toothpaste. Presence of bacteremia in the daily toothbrushing will motivate the orthodontists to follow our recommendations and instructions to protect their patient's lives.

The present study evaluates the performance of two types of oral antiseptics to be used by orthodontic patients in toothbrushing in order to decrease the number of oral bacteria thus decreasing the incidence of bacteremia and bacterial endocarditis. Since little prospective longitudinal information exists on the effects of oral antiseptic therapy in toothbrushing in orthodontic patients, it seems plausible that the use of chlorhexidine mouthwash and antimicrobial toothpaste in toothbrushing is a valuable tool.

In addition, this comprehensive study can provide the clinician with scientific basis for deciding on the treatment of choice for a given patient based on specific criteria.

8. SUBJECTS AND METHODS

8.1 Selection Criteria

Forty healthy adult patients 13 females and 27 males with a mean age of 21.5 years were selected from the clinical intake of the orthodontic department in the dental faculty of Marmara University. They were selected according to the following criteria: The patients were adults with no history of rheumatic fever, rheumatic heart disease, congenital heart defects, cardiac surgery (prosthetic valves), sickle cell disease, arteriosclerotic heart disease, or hematologic disorders. Patients were rejected if they had taken antibiotics or had a history of cold within the last 30 days (Tables 8.1 and 8.2). All patients stated that they were in good general health. All the procedures were explained to the patients and each individual signed an informed consent form as soon as they decide to participate in this research. Once these criteria were fulfilled, the patients were asked about whether they like to volunteer in this research. They were instructed not to brush their teeth, eat, or chew gum or hard candy for 4 hours before their appointments for the blood drawing, and every patient was given a new toothbrush.

Inclusion Criteria
Fixed appliances in both upper and lower jaws, bands on molars and bonded brackets on remaining teeth.
Individuals with a modified gingival index (MGI) <2

Table 8.1 Inclusion Criteria

Exclusion Criteria
Congenital heart disease
History of rheumatic heart fever
Aortic stenosis, mitral stenosis, or both
Prosthetic heart valves
History of subacute bacterial endocarditis
Hypertrophic cardiomyopathy
Surgically constructed systemic-pulmonary shunts
Vascular and joint prostheses
Immunosuppression
Diabetes
Bleeding disorders
Pregnancy
Antibiotic usage within past month
Regular use of antiseptic mouthwash

Table 8.2 Exclusion Criteria

8.2 Modified Gingival Index (MGI)

Oral hygiene status of the patients was determined before initiating the experimental procedure. In order to eliminate gingival probing to assess bleeding which by itself may induce bacteremia, we preferred to use the Modified Gingival Index (MGI). Only those individuals with a MGI <2 were included in the study group, with either absence of inflammation, or mild gingival inflammation, slight change in color, little change in texture of any portion of but not the entire marginal or papillary gingival unit. The criteria for MGI is that it eliminates gingival probing to

assess bleeding, and in redefinition of scoring system for mild to moderate inflammation (56).

0: Absence of inflammation
1: Mild inflammation, slight change in color, little change in texture of any portion of but not the entire marginal or papillary gingival unit
2: Mild inflammation criteria as above but involves the entire marginal or papillary gingival unit
3: Moderate inflammation: glazing, redness, edema and or hypertrophy of the marginal or papillary gingival unit
4: Severe inflammation: marked redness, edema and or hypertrophy of the marginal or papillary gingival unit, spontaneous bleeding, congestion or ulceration.

Table 8.3 Scoring Criteria for the Modified Gingival Index (MGI)

8.3 Experimental Procedure

This study was carried out in 4 groups, each group comprised of 10 patients, wearing fixed orthodontic appliances both on the upper and lower teeth. The first group was considered the control group; bacteremia was measured after toothbrushing without using any tooth paste. In the second group, 0.2% chlorhexidine mouth rinse was used before brushing with no tooth paste. In the third group, subjects used a commonly used tooth paste in Turkey. The fourth group used a newly introduced antibacterial tooth paste.

In the control group, a blood sample of 11 mL was obtained from the antecubital vein of the right arm of each patient in the group using a strict aseptic

technique. Patients were then instructed to brush their teeth using a standardized tooth brush with no toothpaste for 3 minutes. Another blood sample was taken within 2 minutes after toothbrushing in the same technique.

In the second group, preoperative blood sample was taken then the patient was asked to rinse his or her mouth with 15 mL of 0.2% chlorhexidine gluconate mouthwash (Klorhex[®], Drog-san, Ankara, Turkey) for 60 seconds, and to brush their teeth without using toothpaste. Then another blood sample was taken using the same blood sampling technique.

In the third group, blood sample was taken then the patients were asked to brush their teeth with a commonly used tooth paste (Ipana[®] Procter & Gamble, Istanbul, Turkey) for 3 minutes, thereafter, another blood sample was taken from the antecubital vein in an aseptic technique.

In the fourth group, blood samples were taken before any procedure, patients then were instructed to brush their teeth for 3 minutes with an antibacterial tooth paste (One Drop Only[®], One Drop Only GmbH, Berlin, Germany). Within 2 minutes after brushing another blood sample was taken.

8.4 Microbiological Analysis

Pre- and post brushing blood samples were microbiologically evaluated. Ten mL of pre- and post-brushing blood samples were aseptically inoculated into blood culture bottles (Signal Blood Culture System, Oxoid Unipath Limited, Hampshire, England) that were connected to a growth indicator device and incubated at 37° for 14 days. Positive results were indicated in the bottles in which the blood and broth mixture had risen above the green locking sleeve of the growth indicator device. Cultures were taken from the positive bottles and plated on agar and blood agar

supplemented with 0.0005% hemin (Sigma Chemicals Co, St Louis, Mo) and 0.00005% menadione (Sigma). These were incubated under aerobic and anaerobic conditions, respectively (Figures 7.1 - 7.8).

Colony morphology, gram staining procedures, standard microbiologic biochemical testing technique, and API 20 strips (bioMerieux, Marcy l'Etoile, France) identified the bacterial colonies. In addition to the Signal blood culture test, the number of bacteria per mL of blood was determined by the pour-plate method that used 20 mL of fastidious anaerobic agar (Oxoid) supplemented with 5% calf serum. Colonies from the pour plate were counted and identified using this procedure.

Chi square test was used to compare the results. Results of each group – intra group- were compared pre- and post-brushing. Comparison between groups was performed (inter group comparison) as well.

Fig 8.1 Disinfection of the cover of broth bottle with alcohol to ensure aseptic technique

Fig 8.2 Inoculation of 10 mL of blood into the broth

Fig 8.3 Insertion of the growth indicator device

Fig 8.4 The One bottle system is formulated to grow aerobic, anaerobic and microaerophilic organisms

Fig 8.5 Positive results

Fig 8.6 Cultures are taken from positive bottles

Fig 8.7 Culture taken from positive sample being plated on both aerobic and anaerobic blood agar

Fig 8.8 Anaerobic cultures are incubated for 2-10 days under anaerobic conditions in anaerobic jar

9. RESULTS

The microbiologic findings of this study can be seen in tables 9.1 and 9.2. The control group where neither toothpaste was used, nor preceded by mouthwash showed no pre-brushing bacteremia, while post-brushing bacteremia was evident in bottles in which the blood and broth mixture had risen above the green locking sleeve of the growth indicator device (figure 9.1). Post-brushing bacteremia was found in 2 patients (20%) of this group. Cultures were taken from the positive bottles and plated on aerobic and anaerobic blood agar, and incubated at 37° for a period of 14 days in order to distinguish the type and number of bacteria.

Fig 9.1 Bottles with positive (right) and negative (left) results.

The microorganism isolated by the pour-plate method from the post-brushing blood sample of the first patient of the control group was *Streptococcus*

salivarius, while the microorganisms isolated from the second patient in the control group were *Streptococcus salivarius* and *Streptococcus mitis*. Although presence of bacteria was evident and we managed to distinguish the type of microorganism, the number of microorganisms was so small that we could not detect any colony or growth to be counted in terms of colony forming factor (CFU).

	Control Group n = 10	Chlorhexidine Group n= 10	Ipana Group n= 10	One Drop Only Group n= 10
Pre-brushing	—	—	—	—
Post-- brushing	20%	—	20%	—

Table 9.1 Percentage of bacteremia

In the second group, the chlorhexidine group, no bacteremia could be detected in both pre- and post-brushing samples, which means that no growth was detected in the growth indicating device attached to the Signal blood culture bottles.

In the third group, the Ipana group, pre-brushing bottles showed no growth, which means that no bacteremia was present, while post-brushing bottles showed bacteremia in 2 patients (20%). The microorganism found was *Streptococcus salivarius* in both patients. Although presence of bacteria was evident, and we managed to identify the type of bacteria, we faced the same situation as in the control group that the number of microorganisms was very small and we could not detect any colony or growth to be counted in terms of colony forming factor (CFU).

The fourth group, the One Drop Only group, showed the same results as the chlorhexidine group, that is no bacteremia could be detected both pre- and post-brushing samples.

	Control Group	Chlorhexidine Group	Ipana Group	One Drop Only Group
Pre-brushing	–	–	–	–
Post-brushing	<i>S. salivarius</i> <i>S.mitis</i>	–	<i>S. salivarius</i>	–

Table 9.2 Microbiologic Analysis

10. STATISTICAL ANALYSIS

10.1 Null Hypothesis Of The Study

1. There is no difference between the control group and the chlorhexidine group at ($P > .05$).
2. There is no difference between the control group and the Ipana group at ($P > .05$).
3. There is no difference between the control group and the One Drop Only group at ($P > .05$).
4. There is no difference between the chlorhexidine group and the One Drop Only group at ($P > .05$).
5. There is no difference between the One Drop Only group and the Ipana group at ($P > .05$).
6. There is no difference between the Ipana group and the chlorhexidine group at ($P > .05$).

10.2 Statistical Analysis of the Results

Results of each group –intra group- were compared pre- and post-brushing, and comparison between groups was also performed –inter group comparison using Chi square.

There was no statistically significant difference between pre- and post-brushing results ($P > .05$).

Although we have differences in the results, with respect to post-brushing bacteremia: positive in the control group and in the Ipana[®] group, and negative in the chlorhexidine and the One Drop Only groups, the difference between the four groups was not statistically significant ($P > .05$).

11. DISCUSSION

11.1 Site of Blood Withdrawal

Beeson et al compared sites of removal of bacteria from the blood of patients with bacterial endocarditis. Quantitative arterial and venous blood cultures were taken from the following peripheral locations: the femoral artery and vein and the antecubital vein as well as the right auricle, vena cava, hepatic, and renal veins. Blood collected from the antecubital fossa had colony counts only slightly lower than arterial blood (2). The femoral vein had appreciably less bacterial invasion and the hepatic vein had the smallest bacterial count. In our study we chose antecubital vein because the blood collected from the antecubital fossa had colony counts only slightly lower than the arterial blood, and to make it easy for the patient.

11.2 Timing of Blood Withdrawal

Berger et al showed that blood cultures taken immediately after extraction were 81.4% positive for bacteria but decreased to only 48.8% in cultures taken 10 minutes after extraction (6).

Cobe found that intravenous inoculations of *α -hemolytic streptococci* in rabbits were recovered in blood cultures taken by means of cardiac puncture at 1 minute and 3 minutes. Minimal amounts were detected at 5 minutes, and none after 10 minutes (17).

Bender et al observed bacteremia immediately after light scaling and 10 minutes afterward. Initial cultures were positive for 30% of subjects tested, but after 10 minutes only 5% of cultures were positive. These researchers also found positive cultures in 48 cases in which instruments had extended beyond the apex

during endodontic therapy. Immediately after manipulation, 31.2% of the subjects had positive cultures, but cultures taken 10 minutes later were all negative (5).

After carefully evaluating these articles, we chose to take blood samples within 2 minutes after toothbrushing to gain more accuracy.

11.3 Blood Volume Sample

Hall et al compared 5 ml and 10 ml blood-volume samples in 50 ml and 100 ml soybean-casein digest broth culture bottles (tryptic soy broth (TSB), Difco Laboratories, Detroit, Mich.) respectively. A larger number of microorganisms was isolated with significant growth of gram-negative bacilli in the 100 ml bottles (44).

Loesche also strongly advocated increasing the volume of blood samples to increase the isolation of bacteria while Tenney et al found a microorganism yield from 7 ml samples 29% greater than from 2 ml samples(58)(83).This supports the theory that the volume of blood cultured is critical in the detection of septicemia. Washington suggested that the volume of blood is relatively more important than the medium or the atmosphere of incubation in the detection of sepsis.

Salventi et al recommended a blood-to-broth ratio of 1:5 to 1:10 (82). According to Reller, a blood-to-broth ratio between 1:2 and 1:5 may result in an overall decreased number of positive cultures, (78).

Following these results, we took 11 mL blood before and 11 mL after toothbrushing in our study that enables us to explore more bacterial distribution without causing discomfort to the selected patients.

11.4 Culturing Medium

Pfaller et al compared conventional TSB blood culture bottles with a combination of TSB and an agar-coated slide attachment (Septi-Chek, Roche

Diagnostic Systems, Montclair, N.J.) in 2662 sets of blood cultures. Significantly more gram-positive and gram negative bacteria were detected in the slide culture bottle than in the conventional bottles. Growth of gram-positive organisms (particularly *Staphylococcus*) was detected in 24 to 48 hours earlier in the slide culture bottle (76).

Henry et al found that Roche Septi-Chek blood culture was superior to the vented brain heart infusion biphasic medium bottle when both were tested in 5121 culture sets (46).

Weinstein et al detected 99.7% of clinically important organisms in TSB with agar slides (BBL Microbiology Systems, Cockeysville, Md.) but only 82% in conventional blood culture systems. It was concluded that the biphasic system was superior to the conventional system, but this group recommended the use of a complementary anaerobe bottle (94).

Weinstein et al in a subsequent study rated the Septi-Check biphasic blood culture system with TSB superior to conventional peptone broth in 6956 filled-blood culture sets. However, the benefit of a paired anaerobic bottle was reemphasized (93).

Thiemke and Wicher found the use of a radiometric blood culture system (Bactec-Johnson Laboratories Inc., Towson, Md.) valuable in early detection of bacteremia (87).

Thompson found the two-bottle Septi-Chek system less expensive than the Bactec radiometric blood culture system (88).

Weinstein et al found the TSB with slide (Septi-Chek) equal to the Bactec in most respects except for the growth of more fungi in the Septi-Chek bottles (95).

We used in our study blood culture bottles (figure 4.4) from (Signal Blood Culture System, Oxoid Unipath Limited, Hampshire, England) that were connected to a growth indicator device and incubated at 37° for 14 days. Positive results were indicated in the bottles in which the blood and broth mixture had risen above the green locking sleeve of the growth indicator device, which is less expensive and gives accurate results in addition to its being an easy system to use.

11.5 Discussion of The Results

Our results reflect the strict aseptic technique which we followed during collection and microbiologic evaluation of the blood samples in order to reduce the risk of contamination. The organisms identified in the postoperative blood samples were members of the oral microflora. As these organisms are not found on the skin or elsewhere under normal circumstances, their presence in the blood samples is not considered to be due to contamination during blood withdrawal. While if some strains of bacteria appear in blood like *Staphylococci*, this would be probably referred to contamination through skin during blood withdrawal. The organisms isolated in the present study, namely *S. salivarius* and *S. mitis* are readily cultivated from dental plaque and saliva. *S. mitis* was shown to make up 15% of the cultivatable flora of the supragingival plaque and 8% of the cultivatable flora of the gingival crevice. While *S. salivarius* was shown to make up 20% of the cultivable flora of the saliva and dorsum of the tongue, and 11% of the cultivable flora of the buccal mucosa.

According to a study by Coulter et al, *streptococci* were most frequently isolated from post-extraction blood and made up about one third of total isolates (18). *S. sanguis* and *S. mitis* are commonly associated with infective endocarditis. In fact, *S. mitis* is the streptococcal species most frequently isolated from patients with infective endocarditis. These species of *streptococci* produce dextrans, which may account for their preferential ability to stick to endocardium of the heart, great vessels, and valves (81). It has been estimated that 400 or more species reside in the subgingival microbiota. In a recent study, Socransky et al observed five major microbial complexes in the subgingival plaque (84). The third complex as described contained the bacteria isolated in the present study, along with *S. oralis*, *S. gordonii*, and *S. intermedius*. Bacteria belonging to first, second, fourth, and fifth complexes were not detected in the present study. Socransky et al showed that

bacterial species in the first and second complexes had a significant association with increasing pocket depth. Because the persons selected for the present study were considered to be periodontally healthy, there was little possibility of isolating bacteria belonging to these complexes.

Schlein et al reported about the master thesis of Petrovitch who used similar techniques to his technique but, did not detect any bacterial growth in blood samples taken from 26 patients. Schlein claimed that Petrovich's study demonstrated the elusive nature and difficulty of isolating bacteria from the bloodstream because of the following factors: (1) the concentration of bacteria entering the bloodstream, (2) the rate of dispersion of circulating bacteria, (3) the site of blood sampling, (4) the time between inoculation and blood sampling, and (5) culturing techniques (6) we have 10 patients in each group. All of these factors were carefully evaluated in our study which was developed with major revisions in blood sampling and culturing techniques to improve the ability to isolate bacteria from the bloodstream to determine whether bacteremia could be detected after toothbrushing in normally healthy orthodontic patients (83).

Several factors in our study may be considered responsible for the recovery of bacteria in blood samples after brushing: (1) favorable timing of the blood sampling (2 minutes after brushing), (2) increased blood-volume sample of up to 10 mL, (3) culturing technique, (4) site of blood withdrawal, (5) aseptic technique, (6) the large number of patients.

The results of this study conflict with the study of Chung et al in two principal areas. First, Chung found positive cultures before the subjects brushed, and, second, aerobes were not recovered in that study. He explained that pre-brushing bacteremia was possibly caused by eating or brushing just before blood-drawing appointments. The patients in the present study were carefully screened to confirm that these activities had not occurred in the 4 hours before their appointments (14).

The present study is unique in the number of patients included in the study; unlike the few previous studies in this field, Schlein et al experimented 20 patients, others 10-26 patients (83). Also this study took several occasions, most of previous

studies used toothbrush without toothpaste and not used chlorhexidine or any antiseptic before toothbrushing, in our study we started the first group- control group- similar to previous studies, and then we decided to simulate the normal situation of the patients (that all the patients brush their teeth with a toothpaste), so we selected Ipana[®], which is a widely used toothpaste among the population in Turkey.

In a retrospective review of the previous studies on bacteremia and oral hygiene procedures, where bacteremia was present in a percentage of oral hygiene procedures, we intended to search the possibilities for decreasing the number of oral bacteria by using antiseptics and oral washes, referring to the previous studies that good oral hygiene and less number of oral bacteria will decrease the prevalence of bacteria entering blood stream, thus we selected the 0.2% chlorhexidine gluconate with proven efficacy in decreasing oral bacteria when used as a mouthwash. Because chlorhexidine could have side effects with prolonged use we added to our research newly introduced toothpaste with antimicrobial effects of natural products, in order to avoid long use of chlorhexidine.

The 20% post-brushing bacteremia resulted following using Ipana[®] toothpaste, showed no difference when compared to the control group that gave the same prevalence (20%), which means that normal toothpaste did not provide an antibacterial protection to the patient.

While using 0.2% chlorhexidine gluconate, decreased the prevalence of post-brushing bacteremia in this study to 0 %, which shows that decreasing the number of oral bacteria indeed decreased the prevalence of bacteremia, the difference was not statistically significant ($P>.05$). However, by increasing the number of patients in further studies, we might reach significant figures.

The use of chlorhexidine can be recommended in patients with moderate to severe oral hygiene problems for a certain period of time and until oral hygiene is managed, thus decreasing the number of bacteria which in turn will decrease the prevalence of bacteremia.

The use of anti-microbial toothpaste showed successful results, none of the 10 patients developed bacteremia after toothbrushing using this toothpaste, although the results were not statistically significant compared to the results of Ipana and control group (20%) ($P>.05$), but they could be promising as the constituents of this toothpaste are of natural products which may have less side effects than the chlorhexidine. In further studies with more patients, it may be possible to reach statistically significant numbers.

Although the information on the ways and means to prevent infective endocarditis in the medical and dental literature is abundant, nearly all reports designate antibiotics as the central mode prophylaxis and concentrate on infective endocarditis originating from dental care. Recent evidence indicates that prophylactically administered antibiotics have less effect on the incidence of the disease than shifts in the susceptible population. Moreover, sizable numbers of bacterial endocarditis are associated with routinely performed activities, such as tooth brushing and mastication, and are not associated with dental treatment per se. Bacterial strains resistant to the administered antibiotics may engender bacterial endocarditis. It is suggested that penicillin-resistant microorganisms are part of the normal flora in at least 7% of the normal population and more in patients who are in frequent contact with antibiotics. Frequent use of antibiotic prophylaxis makes the treatment more expensive and may trigger adverse reactions, such as hypersensitivity, blood disorders, gastrointestinal problems, bacterial resistance, and interactions with other drugs.

Thus looking for topically administered antiseptics, i.e. mouthwashes and antibacterial toothpastes may help to avoid the above mentioned side effects and drawbacks of systemically administered antibiotics in low risk patients, and in dental treatment and oral hygiene procedures that do not require antibiotic prophylaxis according to the AHA. The current guidelines of the American Heart Association on the prevention of bacterial endocarditis do not include a recommendation for antibacterial prophylaxis for "simple adjustment of orthodontic appliances". This lead The Children's Medical Center at Stony Brooks to report

about the two children with congenital cardiac defect in whom bacterial endocarditis developed after such adjustments in 1991 (8).

Fig 11.1 Gingival hyperplasia in a cardiac orthodontic patient

Fig 11.2 Acceptable gingiva in orthodontic patient

We believe that since orthodontic appliances increase the incidence of gingival hypertrophy and make home care procedures more difficult, the subject of transient bacteremia should be discussed with patients who are at risk. These

patients and their parents must be advised of the importance of removing plaque on a daily basis to reduce the incidence of gingival hypertrophy and reduce the accumulation of plaque. Figure 11.1 shows an unacceptable gingival situation in a cardiac orthodontic patient compared to the patient shown in (Figure 11.2) where the gingival situation is relatively under control. In this case we recommend stopping orthodontic treatment of this patient (Figure 11.1) because he is a patient at risk, and having greater chance to experience bacterial endocarditis as a result of home care procedures, if control on gingiva by a periodontist and the patient does not succeed.

It must be emphasized that patients in this study were healthy and performed adequate home care procedures nevertheless they had transient bacteremia after tooth-brushing, so patients at risk will also encounter transient bacteremia and this will have serious complications. Although Chung and Petrovitch found it difficult or impossible to isolate bacteria from the blood of patients after toothbrushing, and they referred this to the efficiency of a properly functioning immune system, we think that was due to their methodology (14) (83).

12. RECOMMENDATIONS TO THE ORTHODONTIST

After this clinical research and the extensive review of the literature, we came up with the following recommendations in order to help the orthodontists to help their patients at risk of bacterial endocarditis:

1. The orthodontist should evaluate the level of risk of the patient and consider consultation with the patient's internist or cardiologist in order to classify the patient within the categories of high, moderate or low risk regarding bacterial endocarditis, and to decide along with the cardiologist the cardiac condition of the patient and whether prophylaxis is recommended or not.

2. When antibiotic prophylaxis is recommended the orthodontist should follow the regimens prescribed by the American Heart Association, and to prescribe the correct dosage and type of prophylactic antibiotic the orthodontist should always follow the latest recommendations by the American Heart Association.

3. When antibiotic prophylaxis is recommended in a particular patient at risk, it is preferable to do all the banding or debanding procedures in the same session. If this was not possible and another session under antibiotic prophylaxis is required, so allow an interval of not less than 14 days between treatment sessions.

4. Topically administered antiseptics, i.e. mouthwashes and antibacterial toothpastes may help to avoid the side effects and drawbacks of systemically administered antibiotics in low risk patients; topically administered antiseptics can be used in dental treatment and oral hygiene procedures that do not require antibiotic prophylaxis according to the AHA. Moreover, the orthodontist should prescribe antibacterial mouth rinses prior to each session.

5. The subject of transient bacteremia should be discussed with patients who are at risk. These patients and their parents must be advised of the importance of removing plaque on a daily basis to reduce the incidence of gingival hypertrophy and reduce or prevent gingival bleeding, the cause of bacteremia from

home care procedures, and the patient should institute prophylactic measures encompassing frequent dental check up.

6. The orthodontist should postpone all orthodontic procedures until the patient's gingiva have reached a state of maximal achievable health. It must be emphasized that patients in this study with adequate home care procedures nevertheless had transient bacteremia after tooth-brushing.

7. The Orthodontist should not undertake procedures likely to entail trauma, and lacerations to soft tissues. The orthodontist should reduce to a minimum the unavoidable trauma to oral tissues during treatment sessions especially if they are being done without antibiotic coverage, and use mouthwash.

8. The orthodontist should be more conscious of the size and sharp edges on the appliance to minimize gingival hypertrophy and mucosal irritation. Special attention should be given to reduce the size of brackets; to smoothing of tubes, hooks, and bracket wings; and to the avoidance of fixed acrylic appliances such as the Haas rapid palatal expander and the Nance palatal button, and the use of direct bonding instead of bands where possible. Additionally, the orthodontist should take into consideration neuromuscular patterns that affect the pressure and posture of the cheek, lip, and tongue along with the effects of mouth breathing on the gingiva. Every session should end by checking using the orthodontist fingers for any sharp edges and extending wires beyond the end of tubes and ligature wires. The patient should be given a supply of covering wax to cover any sharp edge he or she may discover at home, and asked to call immediately for any emergency following orthodontic treatment session.

13. CONCLUSIONS

1. Toothbrushing in orthodontic patients resulted in 20% prevalence of bacteremia, using normal toothpaste or no toothpaste at all. The use of chlorhexidine mouthwash before toothbrushing, and brushing with antimicrobial toothpaste resulted in decreasing the prevalence of bacteremia after toothbrushing, but the decrease was not statistically significant.

2. Bacteremia can result from toothbrushing in orthodontic patients. The prevalence of bacteremia resulting from toothbrushing is higher than that resulting from banding and debanding in orthodontic patients although the American Heart Association recommended antibiotic prophylaxis prior to banding and debanding in patients at risk of bacterial endocarditis.

3. Although daily oral hygiene procedures have a great potential to cause bacteremia, antibiotic prophylaxis can not be recommended on daily basis, due to their side effects. The use of chlorhexidine mouthwashes prior to toothbrushing, and brushing with antimicrobial toothpaste will decrease the number of oral bacteria which is the source of bacteremia.

4. Chlorhexidine mouthwash cannot be used daily for a long time due to its side effects. The antimicrobial toothpaste may be used on daily basis and particularly during orthodontic treatment but still needs further studies to find out possible side effects during daily use, if this is proved to be safe, future for antimicrobial toothpaste could be promising.

5. The use of fixed orthodontic appliances increases the possibility of gingival hypertrophy and plaque accumulation. This leads to increase in the number of bacterial flora present in the oral cavity. Since larger number of bacteria leads to greater prevalence for the formation of bacteremia, maintenance of good oral hygiene is an essential procedure to prevent bacteremia and bacterial endocarditis, especially as the bad oral hygiene is proved to be associated with bacteremia, and this can be achieved by cooperation between the orthodontist,

periodontist, the general dentist and the patient. Patient's role is very important because this requires daily oral hygiene procedures.

6. This study forms a great beneficial link between orthodontics and medicine, the orthodontists should not refuse to treat patients with possibility to have bacterial endocarditis, but should extend their knowledge, be aware of the recommendations in this field, and undertake the required precautions mentioned in this study to protect their patients.

14. APPENDIX

1. Cardiac Conditions Associated With Endocarditis

A) Endocarditis prophylaxis recommended

1) High-risk category

Prosthetic cardiac valves, including bioprosthetic and homograft valves

Previous bacterial endocarditis

Complex cyanotic congenital heart disease (e.g., single ventricle states, transposition of the great arteries, tetralogy of Fallot)

Surgically constructed systemic pulmonary shunts or conduits

2) Moderate-risk category

Most other congenital cardiac malformations (other than above and below)

Acquired valvar dysfunction (e.g., rheumatic heart disease)

Hypertrophic cardiomyopathy

Mitral valve prolapse with valvar regurgitation and/or thickened leaflets

B) Endocarditis prophylaxis not recommended

Isolated secundum atrial septal defect

Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus (without residua beyond 6 months)

Previous coronary artery bypass graft surgery

Mitral valve prolapse without valvar regurgitation

Physiologic, functional, or innocent heart murmurs
Previous Kawasaki disease without valvar dysfunction
Previous rheumatic fever without valvar dysfunction
Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators

2. Dental Procedures and Endocarditis Prophylaxis

A) Endocarditis prophylaxis recommended*

Dental extractions
Periodontal procedures including surgery, scaling and root planning, probing, and recall maintenance
Dental implant placement and reimplantation of avulsed teeth
Endodontic (root canal) instrumentation or surgery only beyond the apex
Subgingival placement of antibiotic fibers or strips
Initial placement of orthodontic bands but not brackets
Intraligamentary local anesthetic injections
Prophylactic cleaning of teeth or implants where bleeding is anticipated

B) Endocarditis prophylaxis not recommended

Restorative dentistry (operative and prosthodontic) with or without retraction cord
Local anesthetic injections (nonintraligamentary)
Intracanal endodontic treatment; post placement and buildup

Placement of rubber dams

Postoperative suture removal

Placement of removable prosthodontic or orthodontic appliances

Taking of oral impressions

Fluoride treatments

Taking of oral radiographs

Orthodontic appliance adjustment

Shedding of primary teeth

*Prophylaxis is recommended for patients with high- and moderate-risk cardiac conditions.

3. Prophylactic Regimens for Dental, Oral, Respiratory Tract, or Esophageal Procedures

Situation	Agent	Regimen
Standard general prophylaxis	Amoxicillin	Adults: 2.0 g; children: 50 mg/kg orally 1 h before procedure
Unable to take oral medications	Ampicillin	Adults: 2.0 g IM or IV; children: 50 mg/kg IM or IV within 30 min before procedure
Allergic to penicillin	Clindamycin or Cephalexin† or cefadroxil† or Azithromycin or clarithromycin	Adults: 600 mg; children: 20 mg/kg orally 1 h before procedure Adults: 2.0 g; children: 50 mg/kg orally 1 h before procedure Adults: 500 mg; children: 15 mg/kg orally 1 h before procedure
Allergic to penicillin and unable to take oral medications	Clindamycin or Cefazolin†	Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure Adults: 1.0 g; children: 25 mg/kg IM or IV within 30 min before procedure

IM indicates intramuscularly, and IV, intravenously.

*Total children's dose should not exceed adult dose.

†Cephalosporins should not be used in individuals with immediate-type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillins.

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16. BIOGRAPHY

Born on the 25th of November 1968 in Tulkarem, Palestine. Completed the high school education in 1986, and graduated as a Dental Surgeon in 1991 with a B.D.S. degree from the University of Jordan. In the year 1997 passed the American National Dental Board Exam in Pennsylvania in the United States of America.

SAGLIK BİLİMLERİ ENSTİTÜSÜ MÜDÜRLÜĞÜ'NE

Yüksek Lisans öğrencisi Emad Ahmad HUSSEİN'in, çalışması jürimiz tarafından Ortodonti Anabilim Dalı Yüksek Lisans tezi olarak uygun görülmüştür.

İMZA

Tez Danışmanı : Prof.Dr.Nejat ERVERDİ
Üniversitesi : Marmara

Üye : Doç.Dr. Sibel Biren
Üniversitesi : Prof.Dr.Türker SANDALLI
Yeditepe Marmara

Üye : Prof.Dr.Nazan KÜÇÜKKELEŞ
Üniversitesi : Marmara

Üye : Prof.Dr.Tülin ARUN
Üniversitesi : Yeditepe + Yeditepe Dr. Tugay Işık

Üye : Doç.Dr.Ahu ACAR
Üniversitesi : Marmara

ONAY

Yukarıdaki jüri kararı Enstitü Yönetim Kurulu'nun 12... / 02... / 2004 tarih ve 01... sayılı kararıyla onaylanmıştır.

Prof.Dr.Sevim ROLLAS
Müdür