New Strategy on Prevention and Control of Noncommunicable Lifestyle-Related Diseases Focusing on Metabolic Syndrome in Japan

Shunsaku Mizushima and Kazuyo Tsushita

Abstract A new strategy on prevention and control of noncommunicable lifestyle-related diseases focusing on metabolic syndrome, comprising mandatory health assessment and a lifestyle modification advice program aimed at reducing obesity, was undertaken in 2008 by health insurers for the 40–74-year-old insured population, in accordance with a new law of health care access for the aged enforced in 2008. In the standard Health Assessment and Lifestyle Modification Advice Program, the risk is stratified in four determined by the results of health checkups and questionnaires. Accordingly, health information, motivational advice on lifestyle modification, and an active Intensive Lifestyle Modification Program are offered depending on individuals' assessed health risk. The Ministry of Health, Labor and Welfare of Japan estimate that the percentage of the population who would need support offered by the new program is 36.4% of 40–64-year-old males (11.8% motivation support, 24.6% Intensive Lifestyle Modification Program), 27.6% of 65–74-year-old males (motivation support only), 16.2% of 40–64-year-old females (10.2% motivation support, 6.0% active support), and 15.2% of 65–74-year-old females (motivation support only), i.e., approximately twice as many males as females.

S. Mizushima (✉)
Department of Epidemiology and Public Health, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa, Yokohama 236-0004, Japan
e-mail: shunsaku@yokohama-cu.ac.jp

K. Tsushita
Comprehensive Health Science Center, Aichi Health Promotion Foundation, 1-1 Gengo-yama, Morioka, Toura-cho, Chita, Aichi 470-2101, Japan
e-mail: k-tsushita@grp.ahv.pref.aichi.jp

T. Muto et al. (eds.), *Asian Perspectives and Evidence on Health Promotion and Education*, DOI 10.1007/978-4-431-53889-9_4, © Springer 2011

1 Introduction

Japan was ranked best in the world for longevity, disability-adjusted life-years, and quality-adjusted life-years in the World Health Report 2000. In striving to achieve a still healthier nation, Japan has been conducting a population-based national health promotion strategy known as "Health Japan 21" (*Kenko Nippon 21*) since 2000, which consists of 70 targets in seven fields, following on from the First Japan Health Promotion Activity (1978) and the Second Health Promotion Activity (1988). Also, Japan has conducted several strategies for the prevention and control of noncommunicable diseases through secondary prevention activity, such as periodical health checkups; screening for hypertension, diabetes, and dyslipidemia; and use of electrocardiograms and chest X-rays to assess individuals' health risk for cardiovascular diseases such as stroke and ischemic heart disease.

The Ministry of Health, Labor and Welfare conducted a systematic registration to offer this opportunity to the whole populations. Insurance providers have thus offered checkups for noncommunicable lifestyle-related diseases based on the Health Insurance Law, employers have provided employees with physical checkups based on the Industrial Safety Health Law, and local municipal authorities have conducted checkup regimes for citizens aged 40 years or over based on the Laws of Health and Medical Service for the Aged.

Historically, Japan has successfully conducted primary and secondary prevention measures for the prevention of stroke, mainly of hemorrhage type caused by poor diet and hypertension, which was the leading cause of death from 1960 until 1980. Nonetheless the most recent results of interim assessment of Health Japan 21 show an increase in the number of diabetic patients and borderline obesity (in males, 20–60 years old), a decrease in intake of vegetables, and a decline in walking on a daily basis.

A new mandatory health assessment and lifestyle modification advice program focusing on metabolic syndrome was begun in 2008 by health insurers for the 40–74-year-old insured population and their dependents in accordance with a new law of health care access for the aged enforced in 2008. In the standard Health Assessment and Lifestyle Modification Advice Program the risk is stratified in four ranks, determined by the results of physical checkups and questionnaire. Accordingly, depending on individuals' assessed health risk, they are offered health information, motivational advice for lifestyle modification, and an Intensive Lifestyle Modification Program.

The Ministry of Health, Labor and Welfare has estimated the percentage of the population needing support offered by the new program to be 36.4% of 40–64-year-old males (11.8% motivation support, 24.6% active support), 27.6% of 65–74-year-old males (motivation support only), 16.2% of 40–64-year-old females (10.2% motivation support, 6.0% active support), and 15.2% of 65–74-year-old females (motivation support only), indicating the number of males to be about double that of females.

2 Outline of Measures for New Lifestyle-Related Diseases in Japan

According to the interim summary of the "Orientation of Lifestyle-Related Diseases Measures in the Future" initiated by the Health Science Council Community-Based Health Promotion Nutrition Task Force (September 15, 2005) [1], the following are the future tasks for the control of lifestyle-related disease.

- Improvement in the method of determination of potential diabetic patients and their lifestyle modification advice
- The need for evidence-based assessment and modification advice
- Improvement in quality of health assessment and lifestyle modification advice
- Proposals for concrete national health strategies and programs
- Development of a data management system to monitor current situations and measure evaluations

For overall improvement it is necessary to foster the measures and meet the issues above with new methodology, building upon the outcomes of past activities. The summary also points out the importance of the population approach [2], which applies these measures across the whole of Japan. Thus the orientation of the promotion of health care and nutrition relies on an effective combination of the population approach and a high-risk approach anchored in health assessment and guidance.

The contents of this summary are reflected in the expert commission for the New Health Assessment and Lifestyle Modification Advice Program [3] held in July and August, 2005, arranged by Ryozo Nagai, the director of University of Tokyo Hospital.

2.1 Lifestyle-Related Diseases Measure Based on Health Insurance Reform

The government and ruling parties committee on Health Insurance Reform held on December 1, 2005 announced the measures for lifestyle-related diseases as the action plan for Health Insurance Reform.

- Clarification of insurers' role regarding prevention of lifestyle-related diseases
- Development of efficient and effective mandatory assessment and guidance for the insured and their dependents
- Standardization of efficient guidance as a national program

Based on Health Insurance Reform, insurers are required to provide 40–74-year-old insured persons and their dependents with assessment and lifestyle modification advice. The purpose of the measure (or policy) is to decrease by 25% patients and potential patients with lifestyle-related diseases such as diabetes and by 2015 as compared to 2008, and to control the increase in (or save on) health care spending

in the mid and long term. To accomplish these purposes, insurers must conduct efficient assessment and offer lifestyle modification advice. Therefore, the important tasks are development of a standardized program, systematic management of data, and establishment of a baseline for commissioned works.

In 2008, based on the Law of Healthcare Access for the Aged, which followed and revised the aim and purpose of the Law of Health and Medical Services for the Aged and the Health Promotion Law, a new health assessment and lifestyle modification advice program and several measures for lifestyle-related diseases was initiated for the insured population and their dependents who are 40–74 years old, headed by insurers as responsible organizations.

3 Standardizing Health Assessment and Lifestyle Modification Advice Program

The expert committee on metabolic syndrome held in April 2005 (headed by Yuji Matsuzawa, the director of Sumitomo Hospital) determined the concept of metabolic syndrome and the diagnosis criteria. To address diabetes and its potential patients, it was decided that it was necessary to develop a new standardized health assessment and lifestyle modification advice program, implementing the new concept of metabolic syndrome.

Intensive work on a detailed study of a standardized health assessment and lifestyle modification advice program, data management, and the baseline for commissioned works was conducted by the committee in 2006, headed by Shigeru Hisamichi, the manager of hospitals in Miyagi prefecture. A provisional plan was proposed for the program. Later In April 2007, the committee announced its plan for the standardized program building upon preparatory measures conducted in Chiba, Toyama, Fukuoka, and validations of related study groups.

At this stage, the committee revised the plan in order to implement the new concept of evidence-based metabolic syndrome. Also, they initiated implementation of the criteria to stratify patients into four ranks according to the degree of risk factors with regard to lifestyle-related diseases. It was recommended that appropriate advice such as information services, motivational support, and active support be provided for patients. Especially for potential diabetics, the advice on lifestyle improvement would be emphasized. In this program, "specified health guidance" includes both motivational support and active support.

3.1 The Components of Health Checkups

For this new assessment system, the components of a checkup are chosen in order to determine whether patients have lifestyle diseases such as diabetes and metabolic syndrome and related conditions (Table 1).

Table 1 Components of the health checkup program

1. Required items
Questionnaire (history of drugs, smoking, etc)
Physical measurement (height, weight, body mass index, AC)
Physical examination
Blood pressure
Blood test
Lipids (triglyceride, HDL cholesterol, LDL cholesterol)
Blood sugar (FBS or HbA1c)
Hepatic function (GOT, GPT, γ-GTP)
2. Detailed items
Electrocardiogram
Fundoscopy
Anemia test (RBC count, hemoglobin, hematocrit)

Conducted for a condition determined at a physician's discretion
AC abdominal circumference, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *FBS* fasting blood sugar, *GOT* glutamate oxaloacetic transaminase, *GPT* glutamate pyruvate transaminase, *γ-GTP* gamma-glutamyl transpeptidase, *RBC* red blood cells

The new assessment system for the determination of metabolic syndrome introduced measurement of abdominal circumference. Blood pressure is to be measured according to the averaged value of double measurements. In addition, the procedure of blood pressure measurement should conform to the "Cardiovascular Preventive Handbook" (*Hoken-Dojin-sha*) [4] published by the Japanese Association for Cardiovascular Disease Control (JACD).

3.2 *Selecting and Ranking the Patients*

In the new advice program, the patients are ranked according to their risk factors for lifestyle-related diseases. After determination of ranking, patients are provided with advice comprising the components Information Service, Motivational Advice for Lifestyle Modification, and the Intensive Lifestyle Modification Program (Fig. 1). The Information Service for maintenance and improvement of health or appropriate lifestyle is offered to those who have no risk factors. Motivational Advice for Lifestyle Modification is offered to those who have a few risk factors. For those who have multiple risk factors, physicians, public health nurses, and registered dietitians would aggressively conduct the Intensive Lifestyle Modification Program (3–6 month assignment) and support participants in improving their lifestyle, including factors such as physical activity, diet, and smoking cessation (Table 2).

Specifically, the participants noted in step 1 are those who have a waist circumference above standard (male 85 cm, female 90 cm) or who have a body mass index higher than 25 kg/m^2. Participants are considered as step 2 if they have risk factors regarding blood sugar, lipids, and blood pressure, and if they are smokers. For step 3, patients are classified according to the results of steps 1 and 2.

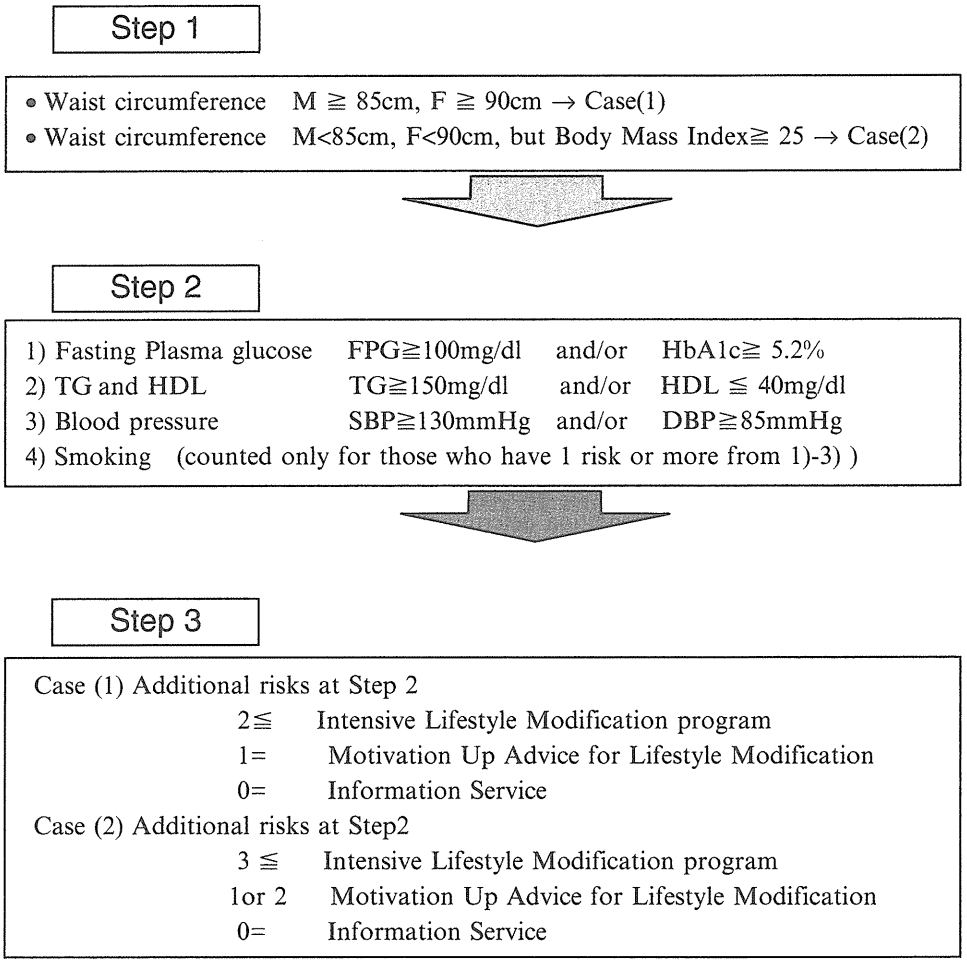

Fig. 1 Classification of participants for the Lifestyle Modification Program

Table 2 Intensive Lifestyle Modification Program: list of intervention points

Support type	Time	Points
Interview and consultation	5 min	20
Group working	10 min	10
Phone call A (consultation)	5 min	15
Phone call B (only encouragement)	5 min	10
e-mail A (consultation)	Interactional sequence	40
e-mail B (only encouragement)	Interactional sequence	5

In step 4, patients in step 3 who correspond to any of the following are offered only motivational support, considering the priority of specified health guidance:

1. Patients who are already affected by lifestyle-related disease and have been on medication should not be included this program over again.
2. Younger elderly patients (65–75 years) who need the Intensive Lifestyle Modification Program are to be offered Motivational Advice for Lifestyle Modification.

4 Lifestyle Modification Program

Three programs for lifestyle modification are provided by health insurers based on a standardized program developed by the Standardizing Health Assessment and Lifestyle Modification Advice Program committee.

1. Information Service

Target: Those with fewer risk factors
Aim: To deliver information to prevent lifestyle-related diseases
Contents: General information on health and metabolic syndrome

2. Motivational Advice for Lifestyle Modification (once)

Target: Premetabolic syndrome (MetS)
Aim: To motivate pre-MetS individuals to lose weight in order to prevent progression of MetS
Contents: Feedback on individual results of health checkup; give information about MetS; encourage patients to set goals to be achieved in 6 months; make plans that can be implemented, such as diet and/or physical exercise and/or quit smoking

3. Intensive Lifestyle Modification Program (3–6-month course)

Target: Metabolic syndrome, pre-Mets + smoking habit
Aim: To help patients to reduce visceral fat and to acquire self-control skills
Contents: Basic plan for Motivational Advice for Lifestyle Modification and Intensive Lifestyle Modification Program, with 180 Points or more during 6 months (Table 2)

5 Preliminary Calculation of Persons Who Would Need Support Offered

Table 3 shows the 2004 estimation of persons who would need support offered, as calculated by National Health and Nutrition Examination Survey by the Ministry of Health, Labor and Welfare and the Strategic Measures Program for Metabolic Syndrome. According to this survey the number of patients needing support would be 36.4% 40–60-year-old male patients (Motivational Support 11.8%, Active Support 24.6%), 27.6% 65–74-year-old male patients (Motivational Support only), 16.2% of 40–64-year-old female patients (Motivation Support 10.2%, Active Support 6.0%), and 15.2% of 65–74-year-old female patients (Motivational Support only). The estimated number of males is double that of females.

To meet the purpose of the program, which is to decrease the number of affected patients to the national targeted value for 2011, each insurer should develop the system to conduct efficient assessment and lifestyle modification advice in line

Table 3 Estimation of persons who need Lifestyle Modification Program

Age (years)	Motivational advice for lifestyle modification (%)	Intensive Lifestyle Modification Program (%)	Total (%)
Male			
40–64	11.8	24.6	36.4
65–74	27.6	–	27.6
40–74	15.5	18.8	34.3
Female			
40–64	10.2	6.0	16.2
65–74	15.2	–	15.2
40–74	11.5	4.5	16.0
Male and female			
40–64	11.0	15.2	26.2
65–74	21.0	–	21.0
40–74	13.4	11.5	24.9

Estimated by National Health and Nutrition Examination Survey 2004 by the Ministry of Health, Labor and Welfare and Strategic Measure Program for Metabolic Syndrome

with the health consultation rate and completion rate for support programs for the insured and their dependents, or with an evaluation figure based on (potential) patients with metabolic syndrome.

Patients will be encouraged to realize their health status based on the results of health checkups, and be further encouraged to understand the relationship between lifestyle (diet, exercise, and so forth) and bodily function and metabolism. Therefore, an effective program would enable patients to change the habits that lead to lifestyle-related diseases. The assessment of the measures for lifestyle-related diseases including health checkups and support programs for the insured and their dependents should be conducted objectively by using data such as those given above, database registration, consultation rate, completion rate of support programs, and the improvement rate for metabolic syndrome.

Further, to enable patients to maintain healthy lifestyles after finishing the support programs, it is important to support patients by utilizing a population-based approach for various resources.

6 Conclusion

In the future, insurers will be in charge of conducting health assessment and lifestyle modification advice based on a new standardized program. Since it is estimated that a great number of people would become involved in this new program, it is assumed that outsourcing to private companies would be encouraged. Therefore, it is crucial that an effective program be developed to encouraging

Table 4 Evaluation of health assessment and Lifestyle Modification Program

Medical expenditure by using receipt/consultation rate/executing rate of health advice
Population approach/importance of the interdisciplinary or time-oriented quantitative assessment in line with diversity of sex and age
Degree of necessity for improvement of lifestyles (high, middle, low)
Improvement rate of metabolic syndrome

patients to improve their lifestyles and to establish an appropriate evaluation system. Within this new system it is also important to pay attention to aspects of metabolic syndrome (Table 4).

References

1. Health Science Council Community-Based Health Promotion Nutrition Task Force, Ministry of Health, Labour and Welfare (2005) The orientation of lifestyle-related diseases measures in the future (interim report) (in Japanese). http://www.mhlw.go.jp/shingi/2005/09/s0915-8.html
2. Rose G (1992) Strategy of preventive medicine. Oxford University Press, Oxford
3. Third Meeting of Health Assessment and Life Style Modification Advice Program (materials) (in Japanese). http://www.mhlw.go.jp/shingi/2005/08/s0826-9.html
4. Japanese Association for Cerebro-Cardiovascular Disease Control (2005) Handbook for preventing cerebro-cardiovascular disease (in Japanese). Hokendohjinsha, Tokyo

T. Hanioka, M. Ojima and M. Nakamura (2012). Effects of Smoking and Smoking Cessation and Smoking Cessation Intervention, Periodontal Diseases - A Clinician's Guide, Jane Manakil (Ed.),
ISBN: 978-953-307-818-2, InTech, Available
from: http://www.intechopen.com/articles/show/title/effects-of-smoking-and-smoking-cessation-intervention

5

Effects of Smoking and Smoking Cessation and Smoking Cessation Intervention

T. Hanioka[1], M. Ojima[2] and M. Nakamura[3]
[1]*Fukuoka Dental College,*
[2]*Graduate School of Dentistry, Osaka University,*
[3]*Osaka Medical Centre for Health Science and Promotion,*
Japan

1. Introduction

The three- to four-decade lag between peak in smoking prevalence and subsequent peak in smoking-related mortality was a major factor affecting public awareness of the substantial health hazards of tobacco use in developed countries (Lopez et al., 1994). This factor may be applicable to periodontal disease if this disease is chronically affected by smoking epidemic. We searched the literature electronically and plotted the number of journal articles on association between smoking and periodontal disease with the trend in cigarette consumption (for example, in the USA) and expected trend in periodontal disease epidemic due to smoking by the year group (Fig. 1). Both peaks of expected trend of the disease and the number of journals stand closely in the 1990'.

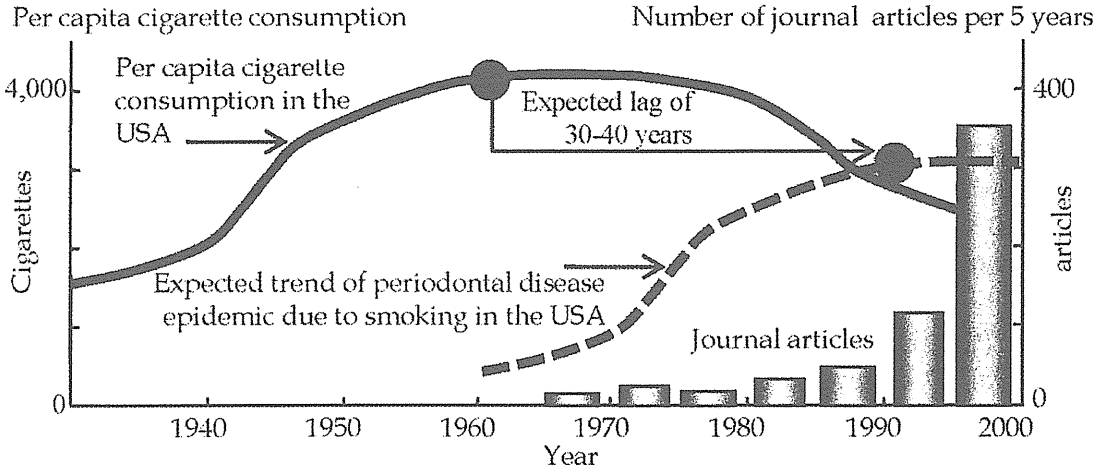

Fig. 1. Application of a descriptive model to the association of increase in smoking prevalence and smoking-related mortality with expected trends in smoking-attributable periodontal epidemic disease. The number of journal articles regarding smoking and periodontal disease followed the increase.

If this factor had been applied at an earlier stage in the series of periodontal research, practice of smoking cessation intervention in dental settings might have been more active.

The lag between the cigarette-smoking epidemic and epidemiological findings on the association of smoking with periodontal disease may have delayed public awareness of this association. Nevertheless, it is now well known that smoking is an independent risk factor of periodontal disease and influences the prognosis associated with periodontal treatments. The validated association in the epidemiologic literature should be biologically plausible, since evidence supporting a causal association between smoking and periodontal disease has accumulated from clinical and basic studies over the past two decades. The underlying mechanism whereby smoking modulates components of the existing etiology of periodontal disease (Page & Kornman, 1997) has been largely clarified (Fig. 2). Though smokers are more susceptible to periodontal disease than non-smokers, bleeding on periodontal probing is less apparent in smokers than in non-smokers. The mechanisms underlying suppression of signs of clinical inflammation in smokers are under consideration for future studies.

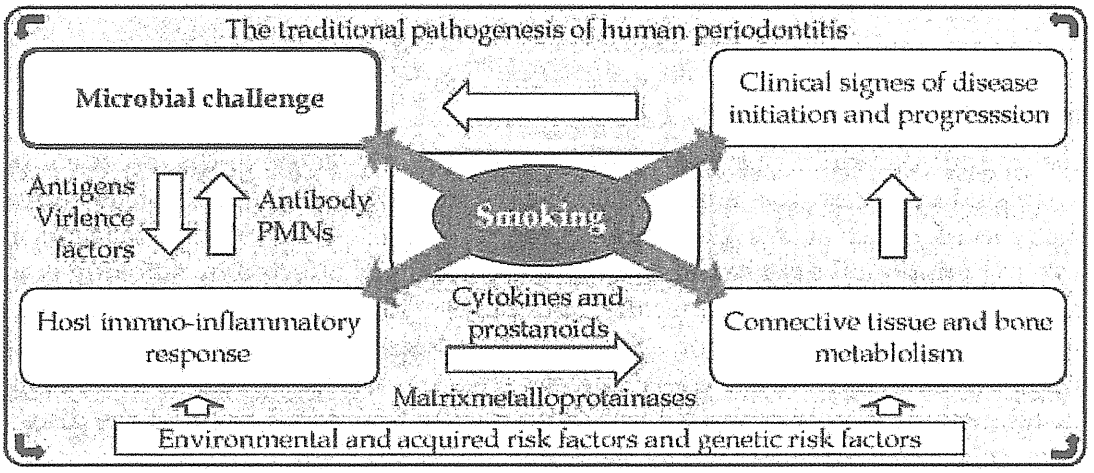

Fig. 2. Mechanisms by which smoking affects periodontal disease based on four components of the traditional pathogenesis of human periodontitis.

Smokers exhibit more periodontal tissue breakdown than non-smokers. These findings are based on the adjustment for confounding factors that are associated with periodontal disease and smoking. The underlying mechanisms include dysfunction of gingival fibroblasts, a decrease in microcirculatory function, and immune system deficiency. The more severe periodontal destruction in smokers than in non-smokers is attributable to impaired ability to repair damaged tissue rather than direct tissue damage.
Deeper understanding was provided by recent progress in molecular and genetic approaches (Ojima & Hanioka, 2010). Smokers exhibited overproduction of inflammatory molecules and suppression of anti-inflammatory molecules, thereby leading to inflammatory destruction of connective tissue and alveolar bone. Very recent studies using a novel method of bacterial identification revealed bacterial involvement in this process and provided an explanation of the connection between smoking and periodontal tissue breakdown in terms of pathogenic periodontal microorganisms.
The results of epidemiological and basic studies have led to periodontal disease now being considered a disease group in which there is sufficient evidence to infer its causal association with smoking. Special attention should be given to the treatment outcomes of periodontal disease in smokers. A negative response to periodontal treatment is consistently reported (Heasman et al., 2006). A more frequent recurrence of periodontal disease in

smokers than in non-smokers during periodontal maintenance was demonstrated (Carnevale et al., 2007). Evidence regarding the effects of smoking on periodontal disease and treatment indicates that smokers lose more tooth-supporting tissue than non-smokers. These effects lead to more rapid loss of tooth-supporting tissue in smokers than in non-smokers. An association between smoking and tooth loss during the periodontal maintenance period has recently been demonstrated (Chambrone et al., 2010). The number of journal articles on the association between smoking and tooth loss, as well as periodontal disease, has increased globally (Fig. 3), and evidence regarding the effect of smoking on tooth loss has accumulated. However, these reports are apparently limited to developed countries, possibly as a result of the lag between the smoking epidemic and occurrence of periodontal disease.

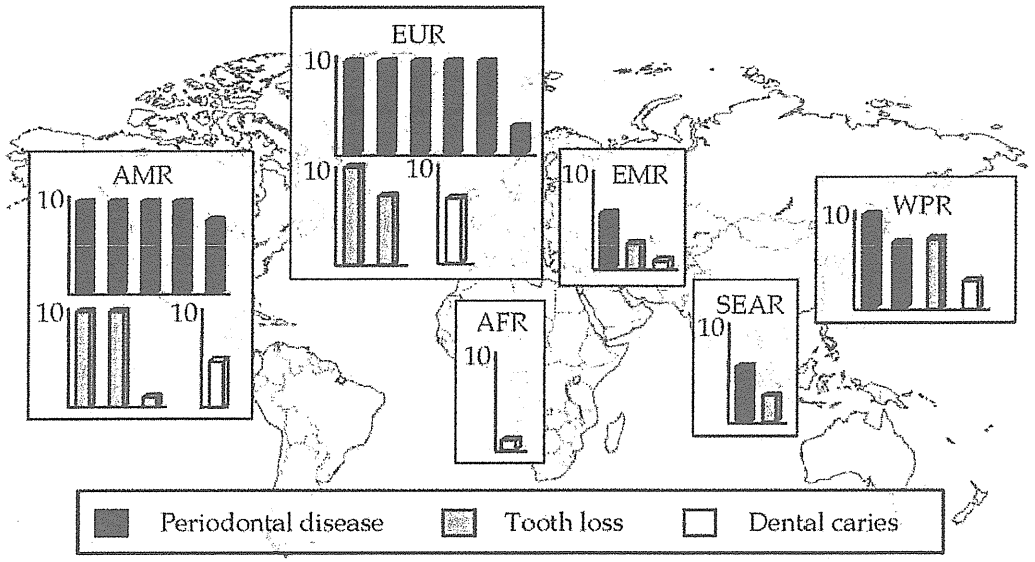

Fig. 3. Number of epidemiological articles addressing the association of smoking with periodontal disease, tooth loss, and dental caries in six WHO regions. The articles were extracted from MEDLINE in 2009 by searching for journal articles on periodontal disease, tooth loss, and dental caries by combining the key words "smoking" or "tobacco," and "periodontal disease" or "periodontitis," "tooth loss," and "dental caries," respectively.

A literature review of observational studies suggests that the evidence supporting a causal association between smoking and tooth loss is strong (Hanioka et al., 2011). Intervention for smoking cessation is an important practice not only for the prevention and treatment of periodontal disease but also for various important oral functions that may depend on the number of existing teeth. Several treatment modalities for tobacco dependence have been considered in the dental setting.

2. Epidemiological evidence

2.1 Periodontal disease and treatment

Effects of smoking and smoking cessation on periodontal disease and treatment responses were examined in observational studies. Data on the effects of adjunctive medications on treatment response in smokers were inconclusive. Benefits of smoking cessation in periodontal treatment were addressed recently.

2.1.1 Increased risk of periodontal disease due to smoking exposure

A comprehensive review in the Surgeon General's Report 2004 concluded that there is sufficient evidence to infer a causal relationship between smoking and periodontal disease (U.S. Department of Health and Human Services, 2004). In addition to studies in the review article, resent studies show a moderate to strong association (odds ratios ranging from 1.4 to 3.5, Warnakulasuriya et al., 2010). The effects on incidence and progression were also elucidated. Dose–response effects also demonstrated that heavy smokers had greater disease severity than light smokers in cross-sectional and cohort studies.

Representative populations were assessed in the USA, Japan, and Australia. The smoking-attributable fraction of periodontal disease ranged from 55.2% to 84% for current smokers and was 21.8% for former smokers. The population-attributable fraction ranged from 12.2% to 60% for current smokers and from 10.9% to 47% for former smokers (Tomar & Asma, 2000; Do et al., 2008). These variations may depend on different characteristics of the population, diversity of surrogate markers of periodontal disease, and confounding variables. An association has also been suggested in developing countries e.g., China, Thailand, and Brazil in terms of the cigarette-smoking epidemic. The consequences of the cigarette-smoking epidemic for oral health extend worldwide.

The effects of smoking on the young population are inconsistent. Smoking was significantly and independently associated with periodontal disease in the young population. A greater apparent association, with an odds ratio of 3.1, was shown in heavy smokers aged 14–29 years (Susin & Albandar, 2005) and in long-term smokers in a birth cohort study, which maintained a high follow-up rate (96%) and had high statistical power with a high incident odds ratio (5.2, Thomson et al., 2007). In contrast, association of smoking with periodontal diseases was not detected possibly due to lack of a sensitive marker such as attachment loss (Ojima et al., 2006).

Second-hand smoke inhalation potentiated bone loss during experimental periodontitis in rats. Data from the National Health and Nutrition Examination Survey (NHANES) III in the USA indicated that individuals exposed to second-hand smoke had greater odds (1.6 times) of having periodontal disease compared to individuals not exposed in the home and workplace (Arbes et al., 2001). Passive smokers, who were identified by salivary cotinine levels, showed a greater number of teeth with clinical attachment loss and higher levels of interleukin-1β, albumin, and aspartate aminotransferase in saliva than counterparts not exposed to passive smoke (Yamamoto et al., 2005). These findings were further confirmed by the research for dose-response relationship (Sanders et al., 2011). Smokeless tobacco users exhibited gingival recession and periodontal disease in the USA, Thailand, Bangladesh, and Sweden.

2.1.2 Decreased risk of periodontal disease due to smoking cessation

Decreased risk of periodontal disease due to smoking cessation is less clearly established than increased risk due to smoking exposure. Some studies suggest periodontal disease severity in former smokers falls between that of current and non-smokers. Very few studies demonstrate a dose–response relationship between risk reduction of periodontal disease and smoking cessation. Findings of the NHANES III revealed that the odds of periodontitis for former smokers who quit ≥11 years previously were indistinguishable from the odds for non-smokers (Tomar & Asma, 2000). In a study of senior employees and retired personnel of the electricity generating authority in Thailand, for light smokers, the odds for severe periodontitis reverted to the level of non-smokers when they had quit smoking for ≥10

years, and for moderate heavy smokers, the odds of having severe periodontitis did not differ from those of non-smokers when they had quit smoking for ≥20 years (Torrungruang et al., 2005).

2.1.3 Effects of smoking on treatment response

The effects of smoking on the response to periodontal treatment have been extensively reviewed (Heasman et al., 2006). A negative effect of smoking on the outcome of several periodontal treatment modalities has been demonstrated in recent studies, and the width of keratinized gingiva for gingival recession therapy, radiographic bone defect, subgingival microbial changes, inflammatory markers, and gingival blood flow in addition to the pocket probing depth, clinical attachment level, and bleeding on probing are used to examine treatment outcome. No significant difference was detected in the 10-year periodontal stability in recession defects of patients receiving guided tissue regeneration therapy and an immediate effect of instrumentation on the subgingival microflora between smokers and non-smokers. Smokers more frequently experienced a recurrence of periodontal disease than non-smokers during supportive periodontal therapy. Tooth loss is a tangible outcome of periodontal treatment and also reflects the recurrence of periodontal disease.

2.1.4 Effects of adjunctive medications on treatment response in smokers

Clinicians are required to use adjunct antimicrobial or host-modulation therapy for smokers. Adjunctive local medications were effective in reducing *Porphyromonas gingivalis*, the attachment level gain reduced with doxycycline, and red or orange-complex bacteria in current smokers and C-reactive protein concentration improved with minocycline. The effects of adjunctive systemic medications, however, are inconclusive. Low-dose doxycycline administration was shown to be effective on analysis of a smoking subgroup (Preshaw et al., 2005a), while no additional benefit was shown in smokers when a stricter analytical method with a multilevel model was used (Needleman et al., 2007). Adjunctive administration did not show an additional benefit compared to non-surgical treatment for azithromycin and surgical treatment for flurbiprofen, while adjunctive azithromycin administration adjunct to scaling and root planing contributed to treatment outcomes in smokers. These findings suggest inconclusive effects of adjunctive medications for smokers, indicating the importance of emphasizing the benefit of smoking cessation.

2.1.5 Benefits of smoking cessation in periodontal treatment

Observational studies comparing periodontal health between current, former, and non-smokers after periodontal treatment suggested that quitting smoking is beneficial to patients with periodontal diseases. Some studies showed that responses to treatment in ex-smokers were similar to those in people who had never smoked. However, there are limited data from long-term longitudinal clinical trials to demonstrate unequivocally the periodontal benefit of smoking cessation. An intervention study investigated longitudinally (12 months) the effect of quitting smoking on periodontal status when combined with non-surgical periodontal therapy in smokers with chronic periodontitis (Preshaw et al., 2005b). A new culture-independent assay for bacterial profiling quantifies the effect on subgingival pathogens. This method revealed an effect on subgingival microbial recolonization after smoking cessation.

Theoretical modeling of the cost-effectiveness of smoking cessation was described. The model revealed that a 10% increase in the number of cigarettes smoked per day increased the treatment costs of periodontal diseases by 0.7% and 0.2% for men and women, respectively (Sintonen & Tuominen, 1989). Adding smoking cessation to the concept of periodontitis prevention will enable significant cost savings to be made.

2.2 Tooth loss

Ten cross-sectional and five prospective cohort studies regarding smoking and tooth loss were selected for the evaluation of methodological quality among 496 citations obtained by a literature search and screening the database. Methodological quality of studies was assessed using a standardized scale; eight studies (six for cross-sectional and two for prospective cohort studies) were classified as high quality.

Three elements—the strength of association, experiment, and the dose-response relationship—were assessed in terms of consistency to allow the synthesis of evidence for each element. The evidence of association was evaluated for each element with respect to consistency through studies that examined 58,755 subjects in four countries; Germany, Italy, Japan, and the USA (Fig. 4). The association between current smoking and tooth loss was significant in all studies. The effect size in cross-sectional studies (odds ratio) varied from 1.69 to 4.04 and that in cohort studies (hazard ratio) was 2.1 and 2.3.

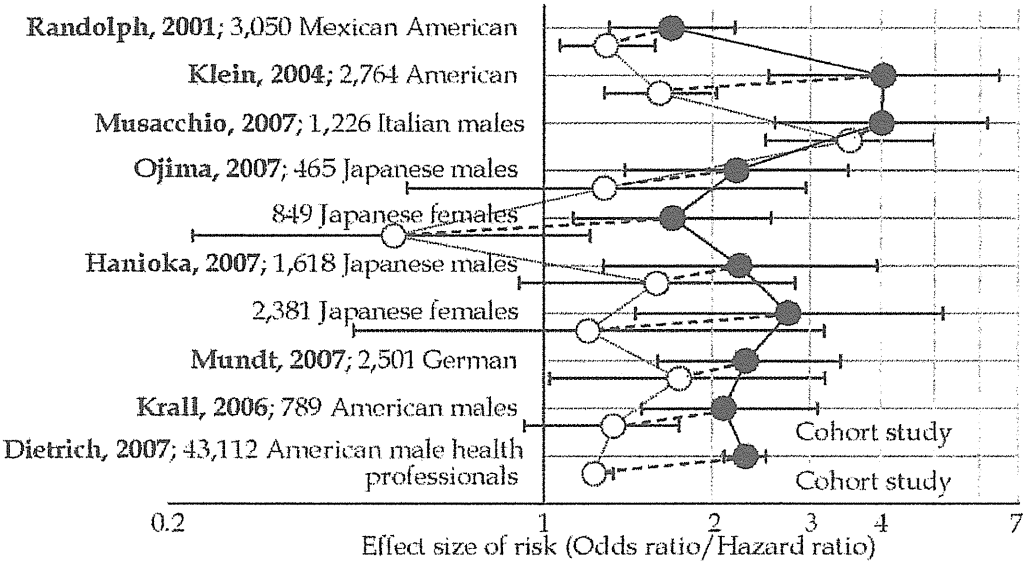

Fig. 4. Effect size (95% confidence interval) of risk of tooth loss in current (closed circles) and former smokers (open circles) relative to non-smokers.

The element of 'experiment' was evaluated by comparing the strength of association between former and current smokers relative to non-smokers, because interventional studies are difficult to conduct in humans. This surrogate element was named "natural experiment." The association between former smoking and tooth loss was not significant in four studies. Although another four studies reported a significant association, the effect size was consistently smaller for former smokers than for current smokers in all studies. The evidence from natural experiments for evaluating the association between smoking cessation and tooth loss was strong with respect to consistency. Two cohort studies with

observational periods of 16 and 36 years on populations in the USA reported decreases in hazard ratios on the basis of years of abstinence (data not shown).

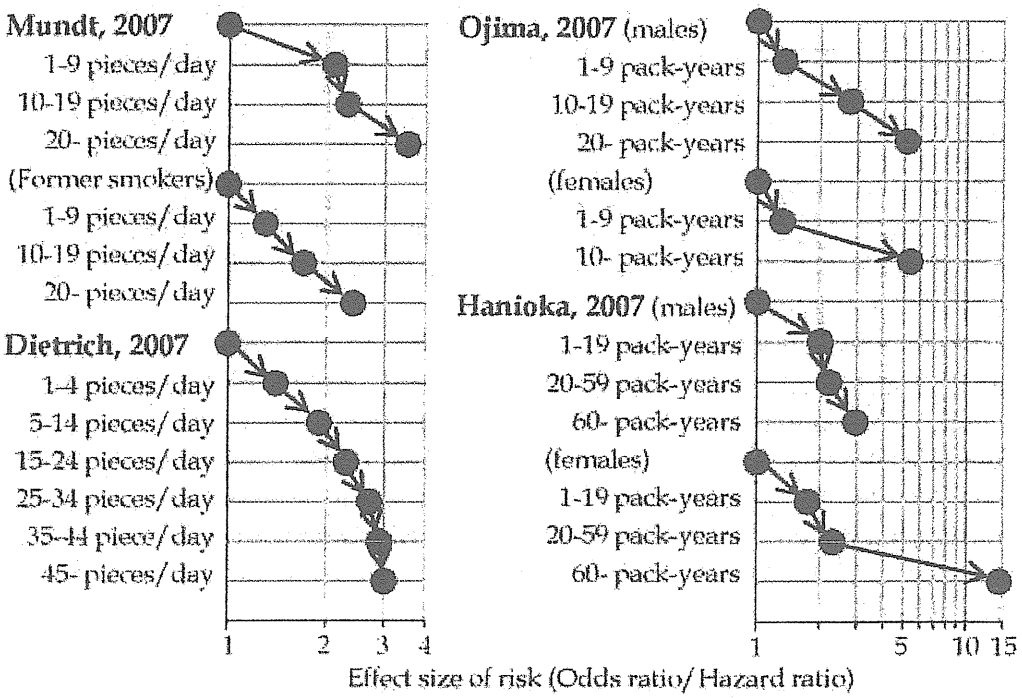

Fig. 5. Relationship between dose of exposure to smoking and effect size.

The dose-response relationship was reported in four high-quality studies, including one cohort study (Fig. 5). These studies examined 50,926 subjects in three countries; Germany, Japan, and the USA. One study in Germany examined the relationship in former smokers. The trend of the relationship between the level of exposure and effect size, i.e., odds ratio or hazard ratio, was obvious in all studies. Therefore, the evidence for a dose-response relationship between smoking and tooth loss was also strong with respect to consistency.
The results from the assessment of each element suggested that the evidence was strong in terms of consistency. This interpretation was based on consistent results with little or no evidence to the contrary in six cross-sectional and two prospective cohort studies. The inclusion of cohort studies indicates more convincing evidence for a causal association. Based on the consistent evidence from each element in the evaluation of this causal association with existing biological plausibility, the evidence supporting a causal association between smoking and tooth loss appears to be strong.

3. Biological plausibility

3.1 Molecular and genetic aspects

3.1.1 Microflora

The effect of smoking on the severity of periodontal disease with respect to the prevalence of specific periodontal pathogens is a controversial issue: some studies have shown differences in the microbial flora between smokers and non-smokers, but several other studies have not been able to demonstrate relevant differences. Differences in periodontal pathogen detection techniques, specimen sampling, and disease definition may explain

these conflicting findings. DNA-based techniques have been employed for the detection of specific periodontal pathogens. The polymerase chain reaction (PCR) is a more sensitive and specific method for the detection of bacteria than conventional culture-based methods.
A series of recent studies (Preshaw et al., 2005b; Delima et al., 2010; Shchipkova et al., 2010) revealed a bacteriological mechanism by using a novel method for bacterial identification. The microbial profile of disease-associated and health-compatible organisms in smoking-associated periodontitis patients was significantly different from that in non-smokers. After non-surgical periodontal therapy and smoking cessation counseling, those who continued smoking had a microbial profile similar to that at baseline, while the subgingival microbiome in those who stopped smoking exhibited a healthy profile. These findings explain the connection between smoking and periodontal tissue breakdown by pathogenic periodontal microorganisms.
Another series of studies (Bagaitkar et al., 2009, 2010; Budneli et al., 2011) addressed the involvement of anaerobic bacterial periodontopathogens in the mechanism of suppression of the clinical inflammatory response in periodontal disease in smokers. As an environmental factor, the stress of cigarette smoke upregulates *P. gingivalis* fimbrial antigens and creates conditions that promote biofilm formation, though the proinflammatory response to the pathogen is inhibited. An reduced inflammatory response potential of oral microflora was indicated by alteration of fatty acid profiles in the saliva of smokers with chronic periodontitis.

3.1.2 Smoking-associated pathophysiological changes

Destructive effects of smoking on periodontal tissue are categorized with respect to vascular, immune, and inflammatory responses (Fig. 6). Smoking modulates the destruction of periodontal tissue through various responses; adverse vascular changes and suppression of host immune systems, and disorder of inflammation (Ojima & Hanioka, 2010).
Repeated vasoconstrictive attacks and impairment of revascularization due to cigarette smoking can influence immune function and the subsequent inflammatory reaction in the gingiva. In the inflamed gingival tissues of smokers, significantly fewer vessels were observed compared to non-smokers. Microcirculatory changes may be related to impairment of oxygen delivery to gingival tissue. Gingival blood flow increased after quitting smoking. Expression of intercellular adhesion molecule-1 (ICAM-1), a marker of endothelial dysfunction leading to damaging vascular disorders, was higher in smokers than in age-matched non-smoking controls. These vascular alterations due to cigarette smoking may contribute to disruption of the immune response and delay in the healing response.
Smoking may depress host immune responses, although there are some conflicting results. The number of neutrophils in gingival crevicular fluid (GCF) was lower or remained constant in smokers compared to non-smokers, while that in blood was higher in a dose-dependent manner. Adverse effects of smoking on the function of polymorphonuclear neutrophils, e.g., reduced viability and phagocytosis, were observed in periodontally healthy smokers. Smoking may influence lymphocyte numbers and antibody production. The serum level of Immunoglobulin G_2 (IgG_2), which was an important antibody against gram-negative periodontal pathogens, decreased in patients with periodontitis. Smoking may decrease the proliferative capacity of T cells or T-cell-dependent antibody responses that affect B-cell function and antibody generation.

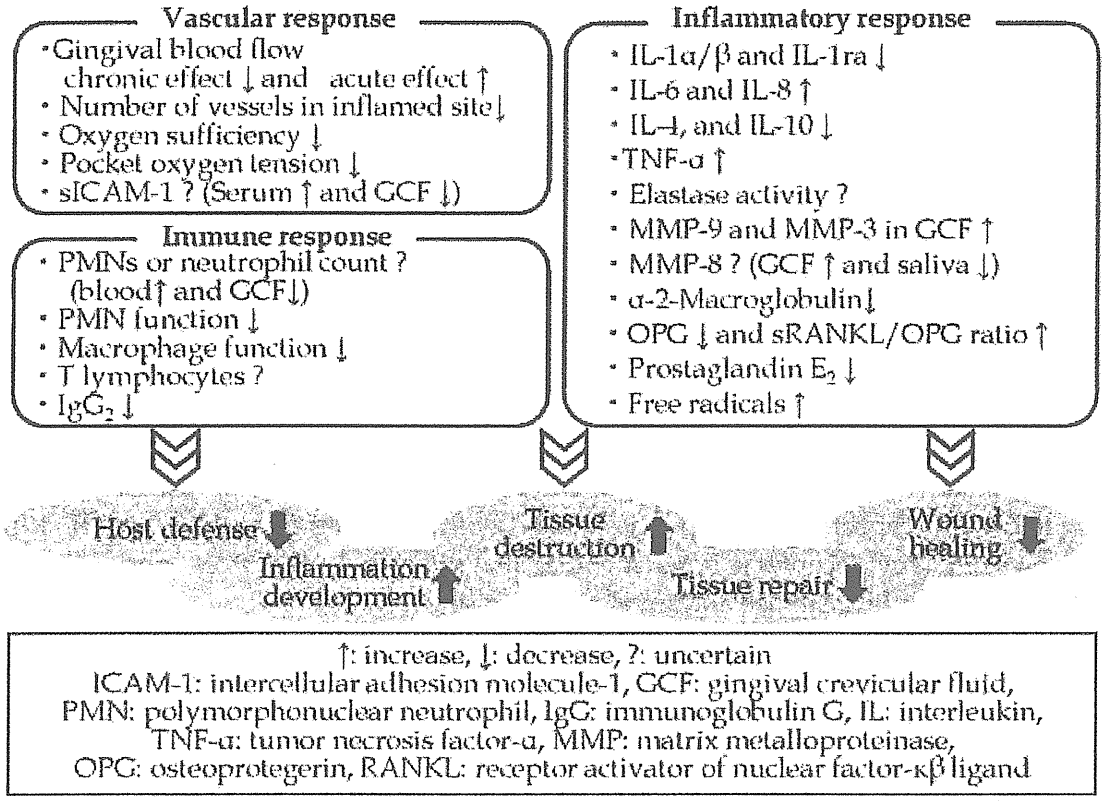

Fig. 6. Destructive effects of smoking on periodontal tissue.

Among several cytokines associated with periodontal disease, levels of interleukin (IL)-1 in GCF have been extensively compared between smokers and non-smokers. Smokers exhibited significantly lower concentrations of IL-1a and IL-1ra in GCF than nonsmokers. Smokers tend to exhibit excess production of inflammatory molecules, such as IL-6, IL-8, and tumor necrosis factor-α, and suppression of anti-inflammatory molecules, such as IL-4, IL-10, and IL-1ra; however, these findings are to some extent inconsistent. Findings regarding the effects of smoking on the level of neutrophil-derived proteolytic enzymes in oral specimens are inconsistent; however, smoking may increase their level in the systemic circulation.

Matrix metalloproteinase-9 (MMP-9) in plasma was higher in smokers than in non-smokers. Smokers had the higher level of elastase and MMP-3 in GCF, and MMP-8 expression in periodontal tissue than non-smokers, while the salivary MMP-8 level was significantly lower in current smokers than in former smokers. Smokers showed a significantly lower concentration of α-2-macroglobulin in GCF as well as total amounts of α-2- macroglobulin and α-1-antitrypsin than non-smokers. Smoking seems to disturb the balance between proteolytic and anti-proteolytic activities in periodontal tissue.

IL-1, IL-6, and TNF-α stimulated the expression of the receptor activator of nuclear factor-κβ ligand (RANKL) and the inhibitor protein osteoprotegerin (OPG), which are dominant regulators of bone resorption and remodeling. The OPG concentration was significantly lower and the sRANKL/OPG ratio was higher in smokers compared with non-smokers, in saliva as well as serum, explaining the greater potential for alveolar bone loss in smokers.

IL-1 and IL-6 induce production of prostaglandin E_2 (PGE_2) by neutrophils and macrophages, which could also accelerate alveolar bone resorption, although the level of PGE_2 in GCF and saliva in smokers was similar to that in non-smokers or even lower than that in non-smokers. The level of free oxygen radicals in periodontal tissues, which induces tissue damage by injuring cells such as fibroblasts, was higher in smokers than in non-smokers. Impairment of fibroblasts by smoking possibly leads to delay in tissue repair and wound healing in periodontal disease.
Most findings support the idea that smokers exhibit a greater burden of inflammatory responses to microbial challenges compared to non-smokers. However, limited evidence is available regarding the effects of quitting smoking on pathophysiological changes in periodontal tissue.

3.1.3 Gene-smoking relationship

Relationships between smoking and genetic susceptibility to periodontal diseases have been investigated with respect to genotypes associated with cytokines (IL-1, IL-6, and IL-10), the immune system (Fcγ receptor), bone metabolism (vitamin D receptor), and xenobiotics metabolism (N-acetyltransferase and myeloperoxidase).
IL-1 polymorphisms have been intensively studied using a cross-sectional design, except for one longitudinal study. Its relationship with respect to smoking is controversial. Several studies reported relationships between IL-1-positive genotypes and smoking; however, other studies demonstrated that the association of IL-1-positive genotypes with the severity of periodontal disease was independent of smoking, suggesting no relationship between smoking and IL-1 genotypes. Logistic regression analysis revealed that odds ratios of periodontal disease, in comparison with IL-1 genotype-negative non-smokers as a reference group, was 0.98 for genotype-positive non-smokers, 2.37 for genotype-negative smokers, and 4.50 for genotype-positive smokers, suggesting synergism between IL-1 polymorphism and smoking (Meisel et al., 2004).
An association between IL-6 and IL-10 genotype and periodontal status was more conspicuous in non-smokers. Fcγ receptors are important components in the binding and phagocytosis of IgG-sensitized cells. Genotypes for Fcγ receptor, FcγRIIa, and FcγRIIIb may be associated with periodontal disease in smokers (Yamamoto et al., 2004). Gene polymorphisms for enzymes that can metabolize smoking-derived substances may contribute to individual susceptibility to the risk of periodontitis among smokers. Subjects with the gene polymorphism for enzymes that can metabolize smoking-derived substances, e.g., cytochrome P450 1A1 M2 allele and the glutathione S-transferase M1 allele, exhibited an increased risk of periodontitis.
To date, gene-smoking relationships in periodontal disease are uncertain because of methodological limitations such as employment of subjects in a specific race, small sample size, and lack of detailed history of smoking and possible confounders. The gene-smoking relationships in periodontal disease may be bilateral; genetic susceptibility to periodontal disease is influenced by exposure to smoking, or the effect of smoking on periodontal disease is influenced by genetic susceptibility. Better understanding of gene-smoking relationship could contribute to the prevention of periodontal disease through personalized recommendation and targeted intervention in public and clinical dental programs.

4. Intervention of smoking cessation

4.1 Dental setting

Smoking cessation intervention is an important category in the dental practice. Smoking cessation intervention is performed in dental setting for a variety of purposes according to the oral condition of patients. Smoking cessation is effective in preventing not only oral diseases but also the progression of periodontal tissue breakdown. Smoking cessation intervention may be integrated in existing procedures of dental treatment because improvement of outcome of the treatment is expected by smoking cessation.

Periodontal practitioners should know the "5 A's" model for treating smoking and nicotine dependence (Fiore et al., 2008a). This model consists of five components for effective smoking cessation intervention: **Ask** about tobacco use; **Advise** about quitting; **Assess** willingness to make a quit attempt; **Assist** in the quit attempt; and **Arrange** follow-up. Although full implementation of the "5 A's" in clinical settings is superior to partial implementation, periodontal practitioners may be responsible for some parts of these components.

Several modalities of smoking cessation intervention have been proposed in the dental setting. The effectiveness of intervention modalities was examined with respect to the success rate of quitting. Since there are several pathways in both the clinical and social setting for smoking cessation, dental practitioners need to know about these pathways to assist patients routinely to choose an appropriate way to succeed in quitting in addition to improving the outcome of dental treatment specific to the patient.

Motivational interview strategies (Fiore et al., 2008a) such as "express empathy," "develop discrepancy," "roll with resistance," and "support self-efficacy" are specialized techniques. Dental hygienists may be able to accept these techniques because they routinely motivate dental patients about oral health behavior on the basis of these techniques. Another strategy that enhances future attempts to quit smoking is the "5 R's" (Table 1).

Relevance	Encourage the patient to indicate why quitting is **personally relevant**, being as **specific** as possible. Motivational information has the greatest impact if it is relevant to a patient's disease status or risk, family or social situation, health concerns, age, gender, and other important patient characteristics.
Risks	The clinician should ask the patient to identify potential negative consequences of tobacco use. The clinician may suggest and highlight those that seem **most relevant to the patient**.
Rewards	The clinician should ask the patient to **identify potential benefits** of stopping tobacco use. The clinician may suggest and highlight those that seem most relevant to the patient.
Roadblocks	The clinician should ask the patient to identify barriers or impediments to quitting and provide treatment that could address barriers.
Repetition	The motivational intervention should be **repeated every time** an unmotivated patient visits the clinic setting. Tobacco users who have failed in previous quit attempts should be told that most people make repeated quit attempts before they are successful.

Table 1. Motivational strategies to enhance attempts to quit smoking; the "5 R's."

The "5R's" strategy is available to dental practitioners. Particularly, four components of "relevance," "risks," "rewards," and "repetition" in the motivational strategies include some issues specific to dental practice. Various oral symptoms and dental treatments relevant to