International Journal of Psychosocial Rehabilitation, Vol. 23, Issue 06, 2019
ISSN: 1475-7192

EFFECTS OF SMOKING

Yashila Periasamy, Saravana Dinesh.S.P, Dhanraj Ganapathy

Abstract
It is well known that smoking contributes to the development of lung cancer and cardiovascular disease, and there is weighty evidence that it has a considerable influence on oral health. Smoking has many negative effects on the mouth, including staining of teeth and dental restorations, reduction of the ability to smell and taste, and the development of oral diseases such as smoker's palate, smoker's melanosis,oral candidiasis and dental caries, periodontal disease, implant failure, oral pre cancer and cancer. From a qualitative point of view the latter is obviously the most serious tobacco-related effect in the mouth. Quantitatively, however, importance has been attached to periodontitis, which affects a large proportion of the population, and during recent years more attention has been given to implant survival rates. As tobacco accounts for such a high proportion of these diseases, comprehensive tobacco control policies are required to make progress in reducing the burden of tobacco-related oral diseases.The present review focuses on smoking-associated oral health problems in older adults, and the steps required for cessation of the habit. Effective treatments to prevent tobacco use and increase cessation are available and need greater implementation. Dental practices may provide a uniquely effective setting for tobacco prevention and cessation.

KEYWORDS: *smoking, tobacco, Pre cancerous lesions, Periodontitis, dental caries*

I. Introduction

Tobacco use is a primary cause of many oral diseases and adverse oral conditions and it is a potent risk factor for many human diseases and conditions including oral cancer, cardiovascular and pulmonary diseases and it has a major deleterious effect on population health. [1] It is one of the major toxic agents in our civilization and its use and smoking is one of the most common causes of mortality and morbidity in developed and developing countries in present times. Tobacco comes from a plant that is native to America, around Peru and Ecuador [2]. It was introduced to Europe from America in the fifteenth century, first being used in medicinal purposes. Later, it came to be burnt in pipes for pleasure on a large scale for nearly 100 years in England and subsequently in Europe as well as the rest of the world. Pipe smoking gave way to the use of tobacco as snuff and in time to cigars and cigarettes varying from country to country, until cigarette smoking became the dominant form in most of the developed countries between the two world wars[2]. Cigarette smoke is highly dynamic and has a complex matrix consisting of a gas phase and a particulate phase with more than 3800 compounds. Among these compounds, 60 of them are well-established carcinogens in animals and 15 of them are carcinogens in humans. Some of the carcinogens found in cigarette smoke include polycyclic aromatic hydrocarbons, aldehydes, arsenic, nickel and cadmium [3]. Smoking not only harms smokers but also harms the people around them. The mechanism of action of cigarette smoke in increasing gingival pigmentation is via the activity of polycyclic amines such as nicotine and benzoperylene that are present in cigarette smoke and enter into the blood circulation following inhalation. They indirectly stimulate the melanocytes. Nicotine also enhances the proliferation of cariogenic bacteria such as mutans streptococci in the oral cavity of smoking mothers and the mothers transfer these bacteria to their infants. Moreover, nicotine decreases the level of vitamin C, which is associated with the proliferation of S. mutans and results in subsequently increased risk of caries. Furthermore, it lowers the saliva pH and decreases the salivary flow and the buffering capacity of saliva while increasing other cariogenic bacteria such as lactobacilli. [4]

Smokers tend to have greater numbers of deeper periodontal pockets and greater mean periodontal probing depth. Studies have also shown greater mean clinical attachment level loss in smokers compared to nonsmokers. [5] The cigarette smoke products in active and passive smoking result in edema and inflammation via the activity of pro-inflammatory agents and local vasoconstriction. Systemically, these products decrease the level of saliva

Undergraduate student, Department of Prosthodontics, Saveetha Dental College,Saveetha Institute of Medical and Technical Sciences, Chennai. Reader, Department of Orthodontics, Saveetha Dental College, ,Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India. Professor &Head, Department of Prosthodontics, Saveetha Dental College,Saveetha Institute of Medical and Technical Sciences, Chennai.
***Corresponding Author**: **Dhanraj Ganapathy**, Professor &Head, Department of Prosthodontics, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Chennai.*

Received: 10 Oct 2019 | Revised: 20 Nov 2019 | Accepted: 02 Dec 2019

IgA and serum IgG and suppress the function of T helper cells in host immunity responses. Moreover, cigarette smoke, via the generation of products such as carbon monoxide and cyanides, delays wound healing and its nicotine content inhibits cell proliferation and osteoblastic activity and stimulates alkaline phosphatase activity. It adversely affects fibroblast activity and decreases the production of fibronectin and collagen by them. Therefore enhancing the knowledge of smokers and creating awareness about the oral and dental problems caused by direct or indirect exposure to cigarette smoke can significantly encourage them to quit smoking.

II. Forms Of Tabacco

Tobacco is the agricultural product of the leaves of plants in the genus Nicotiana. All species of Nicotiana contain the addictive drugnicotine, a stimulant and sedative contained in all parts of the plants except the seeds which occurs in varying amounts depending on the species and variety cultivated.It is used in both smoke and smokeless forms. Smoking forms are more common in western countries while India stands first in the use of smokeless forms of tobacco. Tobacco smoking is the act of burning dried or cured leaves of the tobacco plant and inhaling the smoke. Combustion releases biochemically active compounds in tobacco, such as nicotine and TSNA, and allows them to be absorbed through the lungs.

Smoking Form of Tobacco Usage:

Various Smoking forms of tobacco usage includes: beedis and cigarattes predominantly used with various devices like hooka, hookli, chutta, dhumthi, chillum. Cigarette smokers die younger than non-smokers. It is responsible for more than 430,000 deaths in the United States each year, or one in every five deaths. Cigarette smoking is common in urban areas. However the higher pricing of these products compared to other forms makes this more common amongst the middle and upper socioeconomic classes of population. [6]

Smokeless Forms of Tobacco Usage:

Smokeless tobacco is usually consumed orally or nasally, without combustion. Differents forms of smokeless tobacco are: betel quid chewing, mishri, khaini, ghutka, snuff, and as an ingredient of pan masala. In which snuff and chewing tobacco are majoritily used among people.The smokeless forms of tobacco are Smokeless tobacco is a known carcinogen. Smokeless tobacco users absorb two to three times the amount of addictive nicotine as those who smoke cigarettes. The use of tobacco, especially smokeless forms of tobacco, increases your risk of oral cancer as well, which can be aggressive due to the abundance of blood vessels and lymph nodes in your head and neck.

The Adverse Effects of Tobacco in Oral Cavity

Most people are now aware that smoking is bad for their health. It can cause many different medical problems and, in some cases, fatal diseases. However, many people don't realise the damage that smoking does to their mouth, gums and teeth. The adverse effects of tobacco on oral cavity include oral cancer, precancer, periodontal disease and other mucosal disorders, tooth loss and dental caries.

III. Oral Lesions and Conditions Associated with Tobbaco Use

Leukoplakia

Leukoplakia is a white or gray patch that develops on the tongue, the inside of the cheek, or on the floor of the mouth. Leukoplakia is believed to be a premalignant lesion associated with development of oral cancer . The etiology of OL is considered multifactorial, but smoking is appreciated to be a frequently involved factor. It is much more common among smokers than among non-smokers [7]. Alcohol is thought to be an independent risk factor but definitive data are still lacking. Cross-sectional studies show a higher prevalence rate of leukoplakia among smokers, with a dose-response relationship between tobacco use and oral leukoplakia, and intervention studies show a regression of the lesion after the cessation of smoking . Leukoplakia of the floor of mouth appeared to be significantly more often present in smokers than in non-smokers [8]. Smokers have a six-fold increase in the risk of developing leukoplakia of the oral mucosa regard to non-smokers. The risk factors for malignancy of Oral leukoplakia such as habits (smoking, alcohol intake), clinical form, location of lesions were studied. Among them, tobacco cigarette smoking was reported to be the most important etiological factor for the development of oral premalignant lesions and to their progression into oral carcinoma.

Clinical Features of Leukoplakia

Oral leukoplakia is classified in two main types: homogeneous type which appears as a flat white lesion and non-homogeneous type which includes speckled, nodular and verrucous leukoplakia. The homogeneous leukoplakia is a uniform, thin white area altering or not with normal mucosa. The speckled type is a white and red lesion, with a predominantly white surface. Verrucous leukoplakia has an elevated, proliferative or corrugated surface appearance. The nodular type has small polypoid outgrowths, rounded predominantly white excrescences. Proliferative verrrucous leukoplakia is a subtype of verrucous leukoplakia characterized by an aggressive evolution, a multifocal appearance, resistance to treatment, higher degree of recurrence and a high rate of malignant transformation. [9]

Smoker's Palate and Smoker's Melanosis:

Palatal leukokeratosis (smoker's palate) is an asymptomatic lesion associated with heavy pipe and cigar smoking usually appearing as white changes in hard palate, often combined with multiple red dots located centrally in small elevated nodule. It may disappear after smoking cessation [10]. It does reveal premalignant potential. Smoker's melanosis is increased tissue pigmentation, or darkening, due to irritation from tobacco smoke. Typically this pigmentation occurs on the gingiva of the upper and lower front teeth. The amount of pigmentation increases with greater tobacco use, and is more common in females; it occurs in 5.0 – 22% of cigarette and pipe smokers. There is no treatment for smoker's melanosis; however, tissues typically return to normal colour in six to 36 months after quitting smoking. Melanin pigmentation of the oral mucosa is normally seen in coloured races. Among Caucasian heavy smokers, 30 % prevalence in pigmentation is seen, mostly on the attached gingiva . There are no symptoms and the change is not premalignant . A recent study in the Indian population showed that smokers were more likely to develop smoker's melanosis compared to other lesions [11].

IV. Oral Candidiasis and Hairy Tongue

Cigarette smoke is associated with a variety of changes in the oral cavity and it has an effect on oral commensal bacteria and fungi, mainly Candida species, which causes oral candidiasis. How cigarette smoke affects oral Candida is still controversial [12]. Further studies and research need to find the exact aetiology of smoking and oral candidiasis. It has been seen in the clinical experience that some Candida infections disappear following smoking cessation alone . Another oral lesion, "hairy tongue" or "black hairy tongue" is a benign condition characterized by hypertrophy of the filiform papillae that give the dorsum of the tongue a furry appearance associated sometimes with heavy smoking [13], but its etiology remains unclear. With tobacco use the overgrown papillae can trap pigment from the tobacco and take on a black appearance. This condition has no symptoms; however, it may be a concern due to the appearance and the frequent unpleasant mouth odour from the trapping of particles in the tongue.

Oral Cancer

Use of tobacco products is clearly linked to development of oral cancer. Oral cancer is usually found in the floor of the mouth, the ventralateral surface of the tongue, and the soft palate. Among cigarette smokers, nearly all cancers were found in these locations.Patients with oropharyngeal cancers generally have a 5-year survival of not more than 50 percent. Heavy tobacco users have a 5- to 25-time greater risk of oral cavity and oropharynx cancer. [14]

Cigarette smoking and use of other types of tobacco products cause oral cancer [15]. Oral cancer affects mostly middle aged or elderly people and is more common in men than in women. It constitutes 2-3 % of all cancers worldwide . Cigarette smokers have two to five times higher risk of oral cancer than that of non-smokers the risk increasing with the number of cigarettes and years smoked. On the other hand, cessation decreases the risk . Tobacco-specificN-nitrosamines, aromatic amines, and polycyclic aromatic hydrocarbons presented in mainstream tobacco smoke are considered the major carcinogens contributing to the risk of oral cancer from smoked tobacco products [16].Although the underlying mechanisms are not known in detail, it is said that smoking could lead to cancer because carcinogens in tobacco smoke can induce changes in DNA. In recent years much attention has been given to smoking related mutations in a tumour suppressor gene coding for p53 protein. This protein is important in regulating cell proliferation and has a role in the repair of DNA damage [17]. Smoking-related mutations in the gene may lead to an accumulation of DNA damage in the cells, which may play an important role in the development of cancer.

It has been estimated that between 75 % and 90 % of all cases of oral cancer can be explained by the combined effect of smoking and alcohol use. This could be because alcohol dissolves certain carcinogenic compounds in tobacco smoke and/or because alcohol increases the permeability of the oral epithelium . Smoking and excessive alcohol intake synergistically increases the risk of the development of oral cancer [18].

V. Other Effects on Oral Cavity

Periodontitis

In general, smokers have greater periodontal morbidity than nonsmokers. The vasculature, humoral immune response, cellular immune response, and the inflammatory response may be affected. Nicotine has cytotoxic effects on periodontal ligament fibroblasts. It also has inhibitory effects on periodontal cell proliferation and protein synthesis which result in impaired wound healing. Smoking results in changes to vascular, inflammatory,immune and healing responses. There is considerable scientific evidence of its harmful long term effects on periodontal diseases. It has been reported that smokers do not respond well to periodontal therapy compared to non-smokers and this may be related to the fact that smoking compromises periodontal ligament cell adhesion to root planed surfaces, resulting in the decreased possibility of regeneration. Periodontal diseases, including gingivitis and periodontitis, are common human bacterial infections that affect the gingiva and bone supporting the teeth. Gingivitis is a form of inflammation limited to the marginal gingival tissues, and is usually

caused by the accumulation of dentogingival plaque due to inadequate oral hygiene. Gingivitis is reversible with professional treatment and good oral care at home. Untreated gingivitis may advance to periodontitis under certain conditions when plaque accumulates below the gingival line. Periodontitis refers to the destructive inflammations that result in irreversible loss of periodontal attachment and tooth-supporting alveolar bone [19]. Gingival recession may result from periodontal destruction and exposure of part of the root surfaces of teeth to the oral environment. The exposed root surfaces are at risk of developing root surface caries. Acute necrotising gingivitis is also strongly correlated with tobacco use [20].Although the precise cause of this disease remains unknown; it tends to occur most frequently in teenagers and young adults. Tobacco smoking may exert a masking effect on gingival symptoms of inflammation, which might give smoking patients a false sense of assurance of gingival health [21]. Smoking up regulates the expression of pro-inflammatory cytokines, such as interleukin-1, which contributes to increased tissue damage and alveolar bone resorption [22]. Interleukin-1 genotype positive smokers are more susceptible to severe adult periodontitis [23].

Dental Caries and Saliva

Few studies have shown a relationship between smoking and a higher incidence of dental caries [24,25,26]. There is no evidence of any direct etiological relationship, but the findings of higher counts of lactobacillus and, although various results are reported, Streptococcus mutans in smokers [27] may explain this relationship.

Tobacco usage immediately stimulates salivary flow, but there is no long term effect on saliva flow rates. The pH of saliva rises during smoking, but over longer time periods most studies indicate that smokers have slightly reduced pH and buffering power compared tononsmokers. A recent study showed that smoking is associated with lower salivary cystatin activity and output of cystatin C during gingival inflammation [28].

Peri Implantitis

Peri-implantitis is the formation of deep mucosal pockets around dental implants, inflammation of the peri-implant tissues, and increased resorption of implant surrounding bone. Chronic peri-implantitis results in implant failure when left untreated [29]. Tobacco use may directly compromise the osseointegration of root-form dental implants [30]. The combination of smoking and plaque-induced inflammation significantly influences bone loss around the implants [31] whereas occlusal loading has only a minor role.

Aesthetics, Halitosis and Taste Degeneration

Discoloration of teeth, dental restorations and dentures are very frequent in smokers Discoloration caused by smoking is more severe than that
caused by tea and coffee consumption . Smoking is found to be associated with halitosis [32]. It has been seen that smoking influences the decreased function of smell and it is also associated with worsening of taste perception [33].

Smoking Effects on Oral Microbiota

In addition to periodontal bacteria specifically, smoking may cause changes in the bacteria of plaque in general and affect the host response to the plaque [34]. Nontheless, there are studies published suggesting that not only does smoking not affect subgingival plaque [35], but also that no statistically significant difference is found in the prevalence of any of the bacteria between smokers and non-smokers [36]. A sub gingival bacterium does differ between smokers and non-smokers [37]. Zambon et al. [38] reported that smokers harboured subgingivally significantly higher levels of B. forsythus, whilst Haffajee and Socransky (2001) suggested that the more severe periodontitis in smokers may account for the differences in subgingival bacterial profiles.

Smoking Effects on Oral Host Response

Smoking affects the immune system and impairs host defenses by inhibiting granulocyte function [39]. Subsequent nicotine metabolites cause vasoconstriction and impair the function of polymorphonuclear cells (PMN) and macrophages and decrease the number of lymphocytes which may also affect B-cell and antibody production [40]. Smoking increases the number of neutrophils in peripheral blood but their ability to migrate though capillary walls is dampened because of the paralysis of the cell membrane [41]. PMNs elastase proteinases are released during phagocytosis from the neutrophils [42]. Gingival crevicular fluid levels of functional elastase have been shown to be lower in smokers than non-smokers [43]. Pauletto et al. [44] reported that smoker levels of salivary elastase are lower than those in non-smokers. This might be due to the impaired migration of neutrophils through the gingival crevice to the saliva which, in turn, might cause accumulation of elastase in the periodontium and finally cause tissue destruction. Pauletto et al. [44] further observed that smoking contributes to the activation of monocytes which, unlike PMNs, direct an antigen response to lipopolysaccharides leading to the secretion of cytokines. Of these, prostaglandin PGE2, for example, is linked with aggressive or early onset periodontitis [45]. Nicotine also affects the lifespan and activation of neutrophils reducing their ability to react against bacterial invasion of periodontium. Tobacco and smoking appear to modify

the immune system by exposing B- and T-lymphocytes and thus reducing the production of protective immunoglubulins against oral pathogens [40]. The effects of tobacco on periodontium have recently reviewed by Laxman et al. [42].

Impact of Tobacco Use on Prosthodontic Therapy

The prosthodontist's goal is to provide patient-centered care that meets patient expectations by means that are esthetic, functional, affordable, and predictable. Evidence suggests smoking can compromise a patient's long-term prosthetic outcome whether the prosthesis is natural tooth or dental implant supported. These compromises could relate to tooth loss, ongoing caries management, periodontitis, the need for dental prostheses, the need for ongoing prosthetic maintenance, dental implant failure, periimplantitis, and possibly early prosthetic replacement. In addition, the use of smoked or smokeless tobacco is associated with mucosal changes and an increase risk of oropharyngeal carcinoma. For all the above reasons, patients who smoke should be counseled to cease smoking for their individual oral and systemic health. For those who are partially or completely edentulous, smoking cessation may still reduce the incidence of complications, thereby improving long-term prognosis for prosthodontic care. The best means of eliminating the impact of tobacco on oral health is by never beginning its use.

VI. Some Common Oral Issues Associated with Smoking

Tooth Discoloration

Often the most visible sign of a smoker is yellowing or discolored teeth. In a very quick time, the nicotine and tar can be absorbed by your teeth and take them from white to yellow to brown. Nicotine itself is colourless but when combined with oxygen, it turns yellow. For smokeless tobacco, the tobacco mixes with the saliva and a dark brown liquid is created. This liquid often rests against the teeth for an extended period of time and is extremely staining to the enamel.[41]

Bad Breath

When you inhale a cigarette, smoke particles are left behind in the throat, lungs, and mouth. This can stay in a smoker's mouth for quite some time, leading to the stinky "stale smoker's breath". [44]Smoking and tobacco use can also decrease saliva flow. Dry mouth or xerostomia can lead to a proliferation of bacteria that cause chronic bad breath.

Gum Disease

When using tobacco, plaque tends to accumulate near the gum line rapidly. This affects the attachment of the bone and gums to your teeth. Research shows that specifically smoking interferes with gum tissue cells. The body's immune system is weakened and therefore makes it harder to fight off oral infections. [43]

Tobacco Intervention in Dental Practices

The primary goal is to ensure that every patient who uses tobacco is identified and offered at least a brief intervention at each clinical visit. Following is the summary of the suggested guidelines. [44]

THE FIVE A's IN Tobacco Interception

Ask
Advise
Assess
Assist
Arrange

Ask patients about smoking: A system should be implemented that ensures that every patient at every visit is asked about tobacco use, and the answer documented in the patient's record.

Advise all smokers to stop: The healthcare professional or the dentist should provide the patients with information and advice, reinforcing the patient's own motivation when possible and emphasizing the benefits of stopping. Dentists should demonstrate the oral effects of tobacco if present, or inform patients about the increased risk of poor response or healing after dental procedures relevant to the patient.

Assess the patient's willingness to stop: If the patient is willing to make an attempt to quit, dentists should assist the patient. Dentists should ensure that the patient is aware of the staff's willingness to help, for instance by providing the patient with written information or/and asking the patient in a subsequent visit to reconsider his or her decision.

Assist the patient in stopping: If a patient has a desire to stop, the dentist should help the patient set a realistic quitting date which should be soon but not immediately, so that the patient has time to prepare. If consultation

time is limited, self-help materials that provide the patient with necessary information about smoking cessation can be provided. Nicotine replacement therapy (nicotine gum, inhaler, nasal spray, or skin patch) can be very helpful [45]. Whatever the approach, the dentist should see to it that the patient leaves the office with a concrete plan for stopping and information about how to prepare for the quitting date and how to successfully stop, keeping in mind that most smokers relapse three to five times before succeeding in stopping.

Arrange follow-up contact: Follow-up contacts are very important as the chances of a successful outcome are improved when patients know their progress will be reviewed. The dentist should confirm the quitting date, show continuing support, and follow through if the patient was successful or encourage another try if unsuccessful. If possible the dentist should arrange to see the patients within one or two weeks after the quitting date and consider a second follow-up one or two months later.

It is important that the entire dental team is aware of the relationship between smoking and oral problems. The clinical staff should be familiar with current facts and encouraged to actively participate in tobacco intervention routines.

VII. Conclusion

Periodontal diseases, oral cancers, and precancerous development are linked closely with the tobacco use. Tobacco poses a potential threat to the oral cavity, as they are in direct contact with the mucosal surface. Most of the developing countries including India, have a high exposure to the tobacco products in both the smoke and smokeless forms. Considering the ill-effects with relation to health, it is essential that the usage of tobacco in all forms should be got to a standstill. Hence, it is a role of the clinician to educate the public on this aspect for the benefit of the mankind. Advising patients to quit tobacco use is a dental professional responsibility, and the dentists may take an active role in nicotine replacement counselling. Smoking cessation should be incorporated as an integral teaching component of the undergraduate dental curriculum, particularly with respect to the prevention and diagnosis of tobacco-induced oral lesions and complications. Close collaboration of both dentists and physicians with smoking cessation programmes is advocated in the treatment of tobacco-smoking patients.

References

[1] Musk AW, De Klerk NH. History of tobacco and health. Respirology. 2003 Sep;8(3):286-90.
[2] Doll R. Uncovering the effects of smoking: historical perspective. Statistical methods in medical research. 1998 Apr;7(2):87-117.
[3] Adam T, Baker RR, Zimmermann R. Investigation, by single photon ionisation (SPI)–time-of-flight mass spectrometry (TOFMS), of the effect of different cigarette-lighting devices on the chemical composition of the first cigarette puff. Analytical and bioanalytical chemistry. 2007 Jan 1;387(2):575-84.
[4] Hecht SS. Cigarette smoking: cancer risks, carcinogens, and mechanisms. Langenbeck's Archives of Surgery. 2006 Nov 1;391(6):603-13.
[5] PILLAI HS, JAGANNATHAN N. TOBACCO–A POTENTIAL THREAT TO THE ORAL CAVITY.
[6] Ma N, Tagawa T, Hiraku Y, Murata M, Ding X, Kawanishi S. 8-Nitroguanine formation in oral leukoplakia, a premalignant lesion. Nitric oxide. 2006 Mar 1;14(2):137-43.
[7] Bánóczy J, Gintner Z, Dombi C. Tobacco use and oral leukoplakia. Journal of dental education. 2001 Apr 1;65(4):322-7.
[8] Schepman KP, Bezemer PD, Van der Meij EH, Smeele LE, Van Der Waal I. Tobacco usage in relation to the anatomical site of oral leukoplakia. Oral diseases. 2001 Jan;7(1):25-7.
[9] Johnson N, Bain C. Tobacco and oral disease. British Dental Journal. 2000 Aug 26;189(4).
[10] Reibel J. Tobacco and oral diseases. Medical principles and practice. 2003;12(Suppl. 1):22-32.
[11] Saraswathi TR, Ranganathan K, Shanmugam S, Sowmya R, Narasimhan PD, Gunaseelan R. Prevalence of oral lesions in relation to habits: Cross-sectional study in South India. Indian Journal of Dental Research. 2006 Jul 1;17(3):121.
[12] Soysa NS, Ellepola AN. The impact of cigarette/tobacco smoking on oral candidosis: an overview. Oral diseases. 2005 Sep;11(5):268-73.
[13] Yuca K, Calka O, Kiroglu AF, Akdeniz N, Cankaya H. Hairy tongue: a case report. Acta oto-rhino-laryngologica Belgica. 2004;58(4):161-3.
[14] IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, World Health Organization, International Agency for Research on Cancer. Tobacco smoke and involuntary smoking. Iarc; 2004.
[15] Williams SA, Kwan SY, Parsons S. Parental smoking practices and caries experience in pre–school children. Caries Research. 2000;34(2):117-22.
[16] Winn DM. Tobacco use and oral disease. Journal of dental education. 2001 Apr 1;65(4):306-12.
[17] Nylander K, Dabelsteen E, Hall PA. The p53 molecule and its prognostic role in squamous cell carcinomas of the head and neck. Journal of Oral Pathology & Medicine: Review article. 2000 Oct;29(9):413-25.

[18] Ravald N, Birkhed D, Hamp SE. Root caries susceptibility in periodontally treated patients: results after 12 years. Journal of clinical periodontology. 1993 Feb;20(2):124-9
[19] Johnson BD, Engel D. Acute necrotizing ulcerative gingivitis. A review of diagnosis, etiology and treatment. J Periodontol 1986;57:141–50.
[20] Travis J, Pike R, Imamura T, Potempa J. The role of proteolytic enzymes in the development of pulmonary emphysema and periodontal disease. American journal of respiratory and critical care medicine. 1994 Dec 1;150(6):S143.
[21] Bergström J, Preber H. Tobacco use as a risk factor. Journal of periodontology. 1994 May;65(5s):545-50.
[22] Meisel P, Siegemund A, Dombrowa S, Sawaf H, Fanghaenel J, Kocher T. Smoking and polymorphisms of the interleukin-1 gene cluster (IL-1β, IL-1α, and IL-1RN) in patients with periodontal disease. Journal of periodontology. 2002 Jan 1;73(1):27-32.
[23] Axelsson P, Paulartder J, Lindhe J. Relationship between smoking and dental status in 35-, 50-, 65-, and 75-year-old individuals. Journal of clinical periodontology. 1998 Apr;25(4):297-305.
[24] Hirsch JM, Livian G, Edward S, Noren JG. Tobacco habits among teenagers in the city of Göteborg, Sweden, and possible association with dental caries. Swedish dental journal. 1991;15(3):117-23.
[25] Jette AM, Feldman HA, Tennstedt SL. Tobacco use: a modifiable risk factor for dental disease among the elderly. American Journal of Public Health. 1993 Sep;83(9):1271-6.
[26] Lie MA, Loos BG, Henskens YM, Timmerman MF, Veerman EC, Velden UV, Weijden GV. Salivary cystatin activity and cystatin C in natural and experimental gingivitis in smokers and non-smokers. Journal of clinical periodontology. 2001 Oct;28(10):979-84.
[27] Grossi SG, Skrepcinski FB, DeCaro T, Zambon JJ, Cummins D, Genco RJ. Response to periodontal therapy in diabetics and smokers. Journal of periodontology. 1996 Oct;67:1094-102.
[28] Wallace RH. The relationship between cigarette smoking and dental implant failure. The European journal of prosthodontics and restorative dentistry. 2000 Sep;8(3):103-6.
[29] Lindquist LW, Carlsson GE, Jemt T. Association between marginal bone loss around osseointegrated mandibular implants and smoking habits: a 10-year follow-up study. Journal of dental research. 1997 Oct;76(10):1667-74.
[30] Hoffmann DH. The changing cigarette, 1950-1995. Journal of Toxicology and Environmental Health Part A. 1997 Mar 1;50(4):307-64.
[31] Sato K, Endo S, Tomita H. Sensitivity of three loci on the tongue and soft palate to four basic tastes in smokers and non-smokers. Acta Oto-Laryngologica. 2002 Jan 1;122(4):74-82.
[32] Hilgers KK, Kinane DF. Smoking, periodontal disease and the role of the dental profession. International journal of dental hygiene. 2004 May;2(2):56-63.
[33] Lie MA, Van der Weijden GA, Timmerman MF, Loos BG, Van Steenbergen TJ, Van der Velden U. Oral microbiota in smokers and non-smokers in natural and experimentally-induced gingivitis. Journal of clinical periodontology. 1998 Aug;25(8):677-86.
[34] Stoltenberg JL, Osborn JB, Pihlstrom BL, Herzberg MC, Aeppli DM, Wolff LF, Fischer GE. Association between cigarette smoking, bacterial pathogens, and periodontal status. Journal of periodontology. 1993 Dec;64(12):1225-30.
[35] Kamma JJ, Nakou M, Baehni PC. Clinical and microbiological characteristics of smokers with early onset periodontitis. Journal of periodontal research. 1999 Jan;34(1):25-33.
[36] Zambon JJ. Periodontal diseases: microbial factors. Annals of periodontology. 1996 Nov;1(1):879-925.
[37] Söder B, Jin LJ, Wickholm S. Granulocyte elastase, matrix metalloproteinase-8 and prostaglandin E2 in gingival crevicular fluid in matched clinical sites in smokers and non-smokers with persistent periodontitis. Journal of Clinical Periodontology. 2002 May;29(5):384-91.
[38] Barbour SE, Nakashima K, Zhang JB, Tangada S, Hahn CL, Schenkein HA, Tew JG. Tobacco and smoking: environmental factors that modify the host response (immune system) and have an impact on periodontal health. Critical Reviews in Oral Biology & Medicine. 1997 Oct;8(4):437-60.
[39] Hind CR, Joyce H, Tennent GA, Pepys MB, Pride NB. Plasma leucocyte elastase concentrations in smokers. Journal of clinical pathology. 1991 Mar 1;44(3):232-5.
[40] Lang NP, Lindhe J, editors. Clinical periodontology and implant dentistry, 2 Volume Set. John Wiley & Sons; 2015 Mar 25.
[41] Alavi AL, Palmer RM, Odell EW, Coward PY, Wilson RF. Elastase in gingival crevicular fluid from smokers and non-smokers with chronic inflammatory periodontal disease. Oral Diseases. 1995 Sep;1(3):110-4.
[42] Pauletto NC, Liede K, Nieminen A, Larjava H, Uitto VJ. Effect of cigarette smoking on oral elastase activity in adult periodontitis patients. Journal of Periodontology. 2000 Jan 1;71(1):58-62.
[43] Offenbacher S. Periodontal diseases: pathogenesis. Annals of periodontology. 1996 Nov;1(1):821-78.
[44] Laxman VK, Annaji S. Tobacco use and its effects on the periodontium and periodontal therapy. J Contemp Dent Pract. 2008 Nov 1;9(7):97-107.
[45] Fiore MC. A clinical practice guideline for treating tobacco use and dependence: a US Public Health Service report. JAMA: Journal of the American Medical Association. 2000 Jun.