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Asthma and Oral Health

A Clinical and Epidemiological Study

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Abstract

The oral health of asthmatic subjects was evaluated in this study. In the first phase (Pilot Study) the oral health status and salivary flow rates of 33 adult asthmatics and 33 age and gender– matched controls were compared. Moreover, the saliva composition of 26 asthmatics was compared with that of 33 non-asthmatic subjects. In the second phase (Questionnaire Survey) the occurrence of nine subjective symptoms of oral diseases in adult asthmatics (n = 611) was compared with that of non-asthmatic subjects (n = 606). In addition to the symptoms of oral diseases, information on dietary habits (sugar intake, special diets, use of vegetables) and information on oral health care habits, and general health were evaluated. Moreover, data on background information (education, place of living, smoking history, frequency of alcohol intake, and use of medications), were collected and their role as potential confounding factors was studied.

In the Pilot Study a statistically significant difference between the asthmatics and non-asthmatics was found in the occurrence of inflammatory periodontal disease and in the mean stimulated salivary flow rate. Asthmatics had more periodontal disease and lower stimulated salivary flow rate than non-asthmatic subjects. No major differences were found in saliva composition between the groups.

In the Questionnaire Survey the asthmatic subjects reported more oral diseases than non-asthmatic subjects. In six symptoms out of nine (dry mouth, sore mouth, halitosis, pain in temporo-mandibular joint (TMJ), stiffness in TMJ, and clicking in TMJ), asthmatics had significantly higher probability of having the symptom compared to control group. The underlying cause of TMJ disorders and gingival bleeding was the co-existing allergy. On the other hand, the symptoms of oral dryness could be attributed to the medication used in the treatment of asthma. The latter may also indicate the effect of disease severity rather than the effect of medication itself. In general, subjects having all three risk factors (asthma, allergy and anti-asthma medication) simultaneously, tended to have highest probabilities for symptoms of oral diseases.

Except for the concomitant use of medication other than for asthma, the potential confounding factors studied had only minor or modest effects on the probability of having symptoms of oral diseases. The use of medications was associated with significantly higher probability of having symptoms of several oral diseases when compared to non-users.

The clinical implications of the findings are that the adult asthmatic patients having allergy and regular anti-asthmatic treatment with inhaled medications also need special attention in the oral health care. Co-operation between pulmonologists, asthma nurses and the oral health care team is also warranted.

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Abbreviations

ANOVA	Analysis of variance
BHR	Bronchial hyperresponsiveness
CPITN	Community Periodontal Index for Treatment Need
95%CI	95% Confidence interval
DFS	Sum of decayed and filled surfaces in permanent teeth
DMFT	Sum of decayed, missing and filled permanent teeth
DMFS	Sum of decayed, missing and filled permanent tooth surfaces
dmft	Sum of decayed, missing and filled deciduous teeth
DPI	Dry powder inhaler
ICS	Inhaled corticosteroid
IL	Interleukin
KELA	Social Insurance Institution
OAS	Oral Allergy Syndrome
OHI	Oral Hygiene Index
OR	Odds ratio
PSI	Periodontal status index
pMDI	Pressurized metered dose inhaler
SCI	Sugar Consumption Index
SSFR	Stimulated salivary flow rate
TMJ	Temporo-mandibular joint
TAUH	Tampere University Hospital
Th	T-helper lymphocyte
WHO	World Health Organization

1 Introduction

Asthma has become one of the most common chronic diseases in industrialized countries and its prevalence is increasing throughout the world (von Mutius 2000). Asthma affects all age groups and is often persistent, accounting for a large proportion of health care spending and loss of work (Weiss et al. 1992, Serra-Batles et al. 1998, Sullivan 1998, Szucs et al. 1999).

Relatively few studies exist on the oral health of asthmatic patients. Findings, indicating an increased risk of oral diseases in asthmatic patients are mainly obtained from studies on children and adolescents. According to most published reports, young asthmatic patients suffer more from caries and/or periodontal diseases than non-asthmatic subjects (Hyyppä and Paunio 1979, Hyyppä et al. 1979, Storhaug 1985, Ryberg et al. 1991, Arnrup et al. 1993, McDerra et al. 1998, Kankaala et al. 1998). These findings were mainly obtained from small-scale studies and there are two recently published studies that found no association between dental caries and childhood asthma (Sculman et al. 2001), or association over time between asthma and caries increment (Meldrum et al. 2001).

In their reports Ryberg et al. (1987, 1991) linked the increased incidence of dental caries to the regular use of inhaled β_2-agonists used in the treatment of asthma. However, during the 1990's the treatment of asthma has changed dramatically. Haahtela et al. (1991, 1994) have shown that the regular use of inhaled β_2-agonists is not efficient and the early introduction of inhaled steroids is an internationally approved approach to the treatment of asthma (Global Initiative for Asthma 1995, National Asthma Education and Prevention Program Expert Panel Report 2 1997).

Ryberg et al. (1987, 1991) have also reported differences in salivary flow rate and saliva composition between asthmatic and non-asthmatic children. Saliva plays a major role in the health of the oral cavity (Mandel 1987, Herrera et al. 1988) and any changes in the amount or quality of saliva may alter the oral health status. Saliva contains several defence systems aiming to protect dental enamel and oral mucous membranes. Their effects on the mechanisms of action of various antimicrobial systems and bacterial, fungal and viral species present in human saliva have been extensively studied *in vitro* (Tenovuo 1989, Rudney 1995). However, little is known of their possible significance

in vivo (Gråhn et al. 1988, Nederfors and Dahlöf 1992), and in particular with respect to systemic medication or systemic disease (Herrera et al. 1988, Kirstilä et al. 1994, 1996).

The two most common oral diseases, dental caries and periodontal disease, are preventable to some extent, and early recognition of populations at high risk may help to focus dental health care resources more effectively on the prevention of these diseases. Based on clinical experience, asthmatic patients are also sometimes worried about the possible side effects of inhaled anti-asthma medications on their mouths.

In summary, there exists evidence indicating that asthmatic children, adolescents and young adults may have an increased risk for oral diseases. However, there is only very little information available concerning oral health, salivary secretion, saliva composition, and occurrence of symptoms of oral diseases in adult asthmatics.

2 Review

2.1 Asthma

The traditional definition of asthma was based on functional changes in airway calibre (CIBA Guest Symposium 1959). The definition described asthma as a disease of subjects with widespread narrowing of the bronchial airways, which changes its severity over a short period of time either spontaneously or under treatment, and is not due to cardiovascular disease.

Since that time a lot of data has been gathered about the mechanisms of asthma. The major pathological feature of asthma is considered to be inflammatory changes in the mucous membranes of the airways. The early studies of lung biopsies taken from asthmatic patients showed that inflammatory changes were present already in the very mild form of asthma (Laitinen et al. 1985, Barnes et al. 1988). Based on this information a new definition of asthma was published in 1992 (National Heart, Lung and Blood Institute, National Institutes of Health 1992) in a consensus meeting and was revised in an expert panel meeting in 1997 (National Asthma Education and Prevention Program Expert Panel Report 2 1997). According to the current definition asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular mast cells, eosinophils, T lymphocytes, neutrophils and epithelial cells. In susceptible individuals this inflammation causes recurrent episodes of coughing, wheezing, chest tightness, and difficult breathing, particularly at night and in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyper-responsiveness (BHR) to a variety of stimuli (National Asthma Education and Prevention Program Expert Panel Report 2 1997).

Despite this uniform definition, asthma is a disease with many faces. Allergic asthma is used to describe asthma that is closely related to other allergic diseases like hay fever or allergic conjunctivitis. In fact, atopy – a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop typical symptoms such as asthma, rhinoconjuctivitis and eczema/dermatitis

(Johansson et al. 2001) – is often associated with asthma, and in about 60% of adult asthmatics allergy to one or several environmental allergens (pollen, house dust mite, fungal spores, etc.) can be demonstrated by skin prick tests. Rhinitis is also considered a risk factor for asthma (Leynaert et al. 2000). On the other hand certain chemical agents or dust existing at workplaces may trigger asthmatic symptoms (occupational asthma). Upper respiratory infections also often precede acute deterioration of both allergic and non-allergic asthma (Kava 1987, Gern and Busse 2000). In some individuals the triggering factor may be strenuous exercise (exercise-induced asthma) or simply dry, cold air. Asthma also has a complex genetic background. Linkage, association studies and genome-wide screening suggest that multiple genes are involved in the pathogenesis of asthma (Los et al. 1999, Laitinen et al. 2001).

One important feature of asthma is that even though it is a chronic disease, its severity may fluctuate markedly over time. Asthmatic patients having seasonal allergic rhinitis caused by birch pollen may express asthma symptoms only during a birch pollen period and be almost symptom-free for the rest of the year. Subjects having asthmatic symptoms in childhood may even grow out of the disease and become symptom-free adults (Kokkonen and Linna 1993, Settipane et al. 2000). Taken together, the different types of asthma and the variation in severity of asthma between individuals, a random sample drawn from all asthmatics may lead to a fairly heterogeneous group of asthmatics.

Asthma has gained considerable publicity because of the alarming reports of its increasing prevalence in the industrialised world (Haahtela et al. 1990, Burney et al. 1990, Robertson et al. 1991, Upton et al. 2000). The latest international study reports have shown that the disease affects approximately 3–5% of adult populations and as much as 10% of children (Pearce et al. 2000). However, there is wide variation in asthma prevalence between different countries.

The diagnosis of asthma is based on clinical findings (measurement of lung function or bronchial hyperreactivity) and clinical history of asthma related symptoms (wheezing, breathlessness, cough). The history is particularly important, and in practical management is often sufficiently characteristic to make the diagnosis beyond reasonable doubt. The main symptoms of asthma are shortness of breath, wheezing, tightness in the chest, and cough lasting more than a week. Not all people with asthma will experience every one of these symptoms. In many patients, especially in children, cough rather than

wheezing is the key symptom of asthma. Coughing often occurs during the night or after exercise.

Mechanisms of airway inflammation in asthma involve a cascade of events. Many different cells are involved in asthma: mast cells, macrophages, eosinophils, neutrophils, lymphocytes and platelets. However, it is evident that no single inflammatory cell can account for the complex pathophysiology of asthma, but some cells are more predominant in asthmatic inflammation than others. Mast cells are important in initiating the acute responses to allergen and other causative stimuli. Macrophages derived from blood monocytes may pass into the airways and may be activated by allergens via immunoglobulin E (IgE) receptors. The macrophages produce many different products, including a large variety of cytokines that may orchestrate the inflammatory response (Chung and Barnes 1999).

Cytokines are the hormonal messengers responsible for most of the biological effects in the immune system, such as cell mediated immunity and allergic type responses. T-helper lymphocytes (Th) are the main source of cytokines. T lymphocyte cell subsets have been dichotomised on the basis of their cytokine profiles. In general, Th1 cells produce interleukin (IL) 2 and interferon gamma while Th2 cells produce IL-4, IL-5, IL-6, IL-10 and IL-13. The major function of Th1 cells is to mediate delayed type hypersensitivity. In contrast the major function of Th2 cells is to provide B cell help. The role of all these signalling proteins is not fully understood, but it seems that some of them, like IL-4, IL-5, IL-12 and IL-13, may play an important role in the development of both asthma and allergy (Chung and Barnes 1999). Allergen inhalation results in a marked increase in the number of eosinophils in bronchoalveolar lavage fluid at the time of late response and there is a close relation between the eosinophil count and airway hyperreactivity (Bousquet et al. 1990). Various abnormalities of platelet function have been described in asthma, and animal studies suggest that platelets may be implicated in certain types of airway hyperreactivity, although their role in asthma has not yet been determined (Page 1988, Chung 1997).

At the moment the current treatment strategies in asthma aim at control of symptoms, allowing the patient a normal life. Although the treatment consists of several steps including the avoidance of triggering agents (allergens, certain chemicals etc.) the most important is the control of symptoms with anti-asthmatic medication. A special feature of most asthma medications is the route of administration. Many of the currently used medications are taken as oral inhalations. There are two main delivery systems

available: pressurised aerosols (pMDI) and dry powder inhalers (DPI). In pMDI the medication is stored in a pressurized reservoir canister as a mixture of an active compound and chlorofluorocarbon (CFC) propellant. Recently CFC has been replaced in some cases with hydrofluorocarbon as a propellant. The mixture also contains small amounts of lubricating surfactants. In DPI no propellant is needed and the medication is delivered from the inhaler as a pure medication in powder form or as a mixture of a carrier material, usually lactose or glucose, and active compound. The powder is carried to the lungs with the aid of inspired air. Although the inhalation route offers several advantages over oral administration in the treatment of asthma, it also includes obvious risks for local side effects.

The recommended approach to the pharmacological treatment of asthma is a stepwise approach where the medications used depend on the severity and type of asthma (Table 1). The asthma drugs currently used can be classified into two groups: the relieving drugs used in the treatment of acute asthma attach (bronchodilators) and preventing drugs aiming to suppress the inflammation of mucous membranes in the lungs (anti-inflammatory drugs). During the past ten years there has been a marked shift from the use of relieving drugs as a first line treatment to the use of preventing drugs. The current use of asthma drugs is based on international guidelines (British Thoracic Society 1990, National Asthma Education and Prevention Program Expert Panel Report 2 1997). Because of the inflammatory nature of asthma, regular anti-inflammatory drugs have become the gold standard in the treatment of asthma. The most widely used types of anti-inflammatory drugs are corticosteroids, and especially inhaled corticosteroids (ICS). In their study Haahtela et al. (1991, 1994) showed that ICS are superior to the inhaled sympathomimetics in the long-term treatment of newly detected asthma. ICS are typically used daily in moderate or severe asthma. In the case of poorly controlled or severe asthma, a short course – 7 to 14 days – of an oral corticosteroid such as prednisone may be needed.

Corticosteroids regulate a number of processes in a wide variety of cells but, the exact mechanism of the anti-inflammatory effects is still poorly understood (Bloom 1997). Corticosteroids produce anti-inflammatory responses by modulating gene expression, which in turn leads to a decrease in the amount of inflammatory cells. The effects of corticosteroids are mediated through the corticosteroid receptors located in the cytoplasm. Clinically, by reducing inflammation, they reduce the spontaneous spasm of

airway muscles and decrease the mucous secretion from the mucous membranes of airways (Barnes and Pedersen 1993).

Recently a new class of anti-inflammatory anti-asthma drugs, leukotriene antagonists, have been brought onto the market. The main difference with these drugs from the older ones is both the mode of administration and the mode of action. Two of the drugs – zafirlukast and montelukast – actually block the action of leukotrienes, and a third medication in this class, zileuton, inhibits their production. Antileukotrienes, by themselves are about as effective as theophylline and cromolyn sodium, but if used in combination with inhaled corticosteroids, they may help prevent more attacks. The suppression of inflammation in asthma caused by corticosteroids occurs via different pathways than that of the antileukotrienes.

Bronchodilators open up constricted airways and provide temporary relief. The two main types are β_2-agonists and theophylline. β_2-agonists are typically prescribed for mild, occasional symptoms. The most common drugs, such as salbutamol and terbutaline, act quickly to relieve symptoms and can be used before exercise or exposure to cold air. Prescribed "as needed" they relieve symptoms for up to 6 hours. Inhaled short-acting beta$_2$-agonists do not correct the underlying inflammation. Consequently, they are not long-term solutions and can be easily overused. In 1994 long-acting β_2-agonists (salmeterol and formoterol), became available. They relieve airway constriction for up to 12 hours and are best used for preventing symptoms, especially night time or early morning attacks. Salmeterol and formoterol should be used with an anti-inflammatory inhaler. In fact, the combination of an inhaled corticosteroid and long-acting β_2-agonist can be effective for many people with moderate or severe asthma (Pauwels et al. 1997).

β_2-agonists produce bronchodilation by directly stimulating β_2-receptors in airway smooth muscle, which leads to relaxation. In lungs β_2-receptors are also located in epithelium, submucosal glands and in bronchial vessels. The stimulation of these receptors leads to increased ion transport, increased ciliary function in bronchial epithelium, increased mucous secretion, and reduced plasma extravasation. Side effects of inhaled β_2-agonists are rare. The potential systemic side effects include muscle tremor, tachycardia, hypokalemia, and restlessness. Theophylline is an older bronchodilator that is usually taken daily orally as tablets or syrup. It is especially helpful in relieving night time symptoms. Theophylline may cause nausea, headache or

other side effects. In addition, people taking theophylline should have regular blood tests to ensure the correct dose is given.

In 1994 a national asthma programme was introduced in Finland (Haahtela et al. 2001). In the programme the treatment regimens of international guidelines were adapted to the Finnish health care system, and also to better match the local clinical and scientific experience in the treatment of asthma. This programme also included guidelines for pharmalogical treatment (Haahtela et al. 2000). A brief summary of the recommended asthma treatment in Finland is presented in Table 1.

Table 1. Classification of asthma severity and summary of treatment of asthma according to symptoms and severity.

Severity	Symptoms	Management
Mild intermittent	**Frequency:** Up to twice a week. None between episodes. Night time symptoms less than twice a month. **Duration/effect:** Brief (a few hours to a few days). Intensity may vary.	**Quick relief:** Inhaled short-acting beta2-agonist as needed. **Long-term control:** Inhaled steroid 2-8 week courses
Mild persistent	**Frequency:** More than twice a week but less than once a day. Night time symptoms more than twice a month. **Duration/effect:** Asthma may affect activity level.	**Quick relief:** Inhaled short-acting beta2-agonist as needed. **Long-term control:** Inhaled corticosteroid (low dose) or cromolyn or nedocromil or leukotriene modifiers.
Moderate persistent	**Frequency:** Daily. Daily use of inhaled short-acting beta2-agonist. Night time symptoms more than twice a month. **Duration/effect:** Attacks may last for days. Asthma affects activity level.	**Quick relief:** Inhaled short-acting beta2-agonist as needed. **Long-term control:** Inhaled steroid regularly. If necessary, add a long-acting bronchodilator, low dose theophylline (300-400 mg), or leukotriene modifier.
Severe persistent	**Frequency:** Continuous daytime symptoms, frequent night time symptoms. **Duration/effect:** Frequent attacks. Limited physical activity.	**Quick relief:** Inhaled short-acting beta2-agonist as needed but not to exceed 3-4 times a day. **Long-term control:** Add prednisolone tablets in the morning to the above regimen.

2.2 Oral health and selected symptoms of oral diseases

When trying to measure oral health, one needs to first define what is meant by oral health. Health in general is defined as "a complete state of physical, mental, and social well-being, and not just the absence of infirmity". It is clear that the definition for oral health must include the same components. The oral cavity, i.e. the mouth includes in addition to teeth and gingival tissues, the hard and soft palate, the soft mucosal tissue lining of the mouth and throat, the tongue, the lips, the salivary glands, the chewing muscles and the upper and lower jaws, which are connected to the skull by the temporomandibular joints (TMJ). Thus it is inevitable that oral health is a much broader expression than just healthy teeth. Despite this the sum of decayed, missing and filled teeth (DMFT) has generally been used as an index for oral health, and in the WHO Oral Health Programme it is still one of the main indices. Originally DMFT was introduced for the recording of caries status (Klein and Palmer 1940).

The concept of oral diseases is very complex, ranging from the most usual diseases like dental caries and gingivitis to rare oral symptoms of systemic diseases. The international classification of oral diseases, ICD-DA (WHO 1995) includes over 800 disases and 2000 diagnoses. There are several items in the mouth all contributing to oral health. When measuring oral health we actually need to measure several factors, all of which contribute to oral well-being. From the clinical point of view the measurement of oral health includes both recording of the objectively observed signs of diseases in oral cavity and subjectively reported symptoms of oral diseases.

Self-reported oral dryness (xerostomia) is a relatively common complaint in adult population (Nederfors 1996, Sreebny 2000). Saliva is the key element in the maintenance of oral health (Mandel 1987, Herrera et al. 1988, Sreebny 2000). It initiates the digestive processes and contributes to the maintenance of normal conditions of tissues in the oral cavity and upper part of the gastro-intestinal tract. In the oral environment saliva has several important roles, all of which contribute to the health of the oral cavity. It contains several antimicrobial systems aiming to control the amount of micro-organisms in the mouth (Tenovuo 1989, Rudney 1995). It also lubricates the mucous membranes and protects the teeth from various chemical agents. Saliva has a buffer capacity, which prevents changes in oral pH, protecting the teeth from low pH. The regulation of saliva secretion is a complex system involving at least adrenergic, cholinergic and nonadren-noncholinergic nerves (Suddick and Dowd 1980, Baum et al.

1984, Ekström 1989). Hormonal status and several neuropeptides also affect both the synthesis and secretion of saliva.

In the literature there exist several reasons for xerostomia, including medications, diseases, nutritional status, radiation therapy in head and neck among the most often listed aetiologic factors (Sreebny 2000). It is noteworthy that reported xerostomia does not always correlate with objectively measured decreased salivary flow rate (Fox et al. 1987). Thus other reasons, like increased water evaporation from oral mucous membranes due to breathing through the mouth or possible other pathologic conditions of the oral mucous membranes should also be considered. The decrease in salivary flow rate leads rapidly to the marked impairment of oral health (Loesche 1986, Herrera et al. 1988). Thus in the context of oral health saliva secretion needs special attention.

Sore mouth is usually described as a painful feeling originating in the oral mucose membranes and tongue. There exist several conditions all of which have the potential for leading to oral soreness. The diseases of the oral mucous membranes, tongue and lips consist of a variety of conditions either originating in the oral cavity or oral manifestations of systemic diseases (Scully and Shotts 2000). Infections of the oral mucous membranes are a common reason for lesions seen in the oral mucous membranes. The normal flora contains a variety of organisms, many of them potentially pathogenic. In patients with reduced host defence certain organisms, like *candida albicans* that is present in the oral cavity in almost half of the adult population, may cause pathologic changes in oral mucosa in some individuals (Waal and Pindborg 1986). Viruses, like human papilloma virus and herpes zoster virus, are also often involved in oral mucosal lesions (Chang et al. 1991, Birek 2000, McIntyre 2001). Recurrent oral ulceration is a common disorder found in the oral cavity. The reason for ulcers in the oral cavity may be a simple mechanical trauma caused by a fractured tooth, filling or poorly fitting denture. Decreased salivary flow rate may also predispose oral mucosa to mechanical trauma (Scully and Shotts 2000). Often, as in aphtous ulcers the reason remains unclear, but some kind of disturbance in the autoimmune defence system have been proposed (Porter et al. 1998, Ship et al. 2000). Sometimes patients with clinically healthy oral mucous membranes report burning, painful or itching sensations in oral mucosa (Scully and Shotts 2000). The reasons for this condition are not clear, but this so-called burning mouth syndrome is most typical in post-menopausal women. Proposed causative factors include reduced salivary flow, candida infection,

allergy and even psychogenic factors have been suggested (Lamey 1996, Bergdahl and Bergdahl 1999).

One special condition that may lead to oral soreness is oral allergy syndrome (OAS). OAS is a manifestation of food allergy (Pastorello et al. 1995). It is an allergic reaction that is confined to the lips, oral mucous membranes and pharynx. OAS normally occurs in atopic individuals after eating fresh (raw) fruits and vegetables. The usual symptoms include rapid onset of itching of the lips, mouth, or pharynx and swelling of the lips, tongue, throat and palate. Other symptoms may include gingivitis, conjunctivitis, or rhinitis. Batch testing has therefore been recommended for patients with unexplained oral and perioral symptoms (Shah et al. 1996). Some of the pathologic conditions seen in oral mucous membranes have a potential to develop into malignant diseases like oral cancer. One of the most common precancerous lesions is oral leukoplakia, which has even been used as a surrogate end-point in the epidemiological investigation of the occurrence of oral cancer (Gupta et al. 1990).

Breath malodor (halitosis) is defined as offensive odors emitted from the mouth (McDowell and Kasselbaum 1993). Although halitosis is a common complaint, identifying the exact reason remains a challenge to the dentist and sometimes needs co-operation with an ear, nose and throat specialist (van Steenberghe 1997). The most obvious reasons for halitosis are related to dental plaque and periodontal disease. Plaque organisms like *Porphyromonas gingivalis, fusobacteria*, and other anaerobics accumulating in periodontal pockets are capable of releasing volatile sulphur compounds (Coventry et al. 2000). Pocket formation may also lead to accumulation of food debris and pus may even be expressed. Because of this halitosis is often associated with periodontal diseases (van Steenberghe 1997). The other sources of halitosis may include tongue coating, paranasal sinuses and throat.

Sounds in the TMJ including clicking or grinding sensation in the joint is one of the most widely known symptoms of TMJ disorders. It may be independent or accompanied by: pain in or about the ears, jaw fatigue, soreness or tenderness of the jaw muscles, stiffness of the jaw and even increased attacks of headaches. The TMJ is the joint formed by the temporal bone of skull with mandible. The TMJ is the most complex joint in the human body, actually consisting of two joints, one in front of each ear. The masticatory muscles and several ligaments support this complex structure. TMJ dysfunction syndrome is a disorder of the temporo-mandibular joint and associated masticatory apparatus (Dimitroulis et al. 1995). The aetiology of TMJ disorders is not

well understood and there are several theories about the aetiology of TMJ disorder (McNamara et al. 1995, Mew 1997). Recently, research has also focused on the possible inflammatory changes in the synovial tissues of the TMJ as possible causes of TMJ disorders (Alstergren 2000).

Sensitivity to hot cold and sweet stimulants and toothache are considered classic symptoms of dental caries. The most important aetiological factor in the development of dental caries is the activity of dental bacterial plaque consisting of various microbes, including mutans streptococci and lactobacilli, colonizing in the tooth surfaces. Dental plaque is a soft amorphous layer of mucus that covers hard dental enamel and is an ideal attachment for microbes (Loesche 1986). Fermentation of sucrose and other sugars by bacteria to lactic and other acids causes decalcification of the hard dental enamel and leads to caries. In advanced dental caries, when the lesion has perforated the hard dental enamel there is a possibility that the soft tissues and nerves located in the pulp chamber become irritated leading to inflammation and pulpal pain. In the mild form there are symptoms only in association with certain irritating agents (sweet, acidulous, and sometimes even cold or hot food and drinks) but if the pulp is severely affected the pulpal pain may be spontaneous and strong.

Although caries is the main suspect in toothache and sensitivity, there are also other possible reasons for dental pain. In cases when the tooth is exposed to external stress caused by trauma, occlusal stress (bruxism) or strong wear, sensitivity to certain triggering agents may occur. Pain is quite seldom associated with periodontal disease but sometimes when due to loss of gingival tissues the surface of the root of the tooth is exposed to hot, cold or acidulous triggers transient sharp pain may be felt (Ide 1998). The supposed explanation behind the pain in these cases is hydrodynamic mechanism (Selzer and Boston 1997, Orchardson and Cadden 2002). In hydrodynamic mechanism sudden dentinal pulp fluid movements in the dentinal tubules are believed to stretch certain nerve fibres located in the pulp-dentin interface. Deformation of these nerves leads to short, sharp pain. In the case of deep periodontal pockets, periapical periodontitis may develop leading to abscesses and pain due to inflammation in the periapical region.

Bleeding from the gum is a cardinal sign of inflammatory periodontal disease known as gingivitis (Carranza 1996). Gingivitis is a reversible condition, and if treated, does not always progress to more severe periodontal disease, periodontitis (Coventry et al. 2000). The aetiology of gingivitis is a bacterial plaque cumulated around the teeth

causing an inflammatory response, and the disease is resolved by good plaque control. Gingivitis may lead to an irreversible condition, periodontitis which is a general term used to describe inflammatory disease that destroys the gingival and supporting connective tissue and alveolar bone (Williams 1990). In the final stage abscesses or tooth mobility may occur when a large amount of tissue supporting the tooth has been lost. Periodontal diseases are widely distributed in adult populations but there are variations in disease severity (Albandar and Kingman 1999).

In its early stages gingivitis is almost symptom-free and the most usual symptom is spontaneous bleeding from the gums because of inflammatory changes in the epithelial junction between the gum and the tooth (Williams 1990). Although gingivitis is the most important reason for gingival bleeding, there may also be other reasons like trauma, and haemorraghic tendency due to systemic diseases, or bleeding may follow the administration of excessive amounts of certain drugs like salicylates (Carranza 1996).

2.3 Asthma and oral health – a review of the literature

The possible effects of asthma and/or allergy on oral diseases have not been widely studied, and the number of published reports is fairly limited. However, the association between asthma and dental caries has been evaluated in ten studies (Hyyppä and Paunio 1979, Storhaug 1985, Bjerkeborn et al. 1987, Ryberg et al. 1987, 1991, Arnrup et al. 1993, Kankaala et al. 1998, McDerra et al. 1998, Meldrum et al. 2001, Shulman et al. 2001)

Hyyppä and Paunio (1979) compared the oral health condition and some salivary factors between asthmatic children aged 10 to 12 years and a group of healthy children of the same age. Thirty asthmatics and controls were included. The groups were further divided according to age to younger (10–11 years of age, n = 15) and older (12 years of age, n = 15) subjects. There were no differences in salivary constituents, salivary flow rates or in DMFS scores between the asthmatic and healthy children. In the 12 year age group, the asthmatic children had slightly higher mean DMFS scores compared to the healthy children, 13.1 and 9.8, respectively, but the difference was not statistically significant.

In the study by Storhaug (1985) the parents of 436 disabled pre-school children were interviewed about habits and problems relevant to dental health. The children, who represented 10 different disabling conditions, were examined and dmft registered. The purpose was to study the relationship between different background variables and caries experience. The number of daily carbohydrate intakes, duration of use of nursing bottle, family income and diagnosis were the variables with the strongest association with dmft. Children with congenital heart disease, asthma, and cystic fibrosis had a considerably higher adjusted dmft than the other diagnostic groups. The proportion of children with caries experience was higher in the survey than in groups of Norwegian children of corresponding age.

Oral health was studied in a group (n = 61) of asthmatic children (Bjerkeborn et al. 1987). The children were divided into two groups, 5–10 and 11–18 year olds. The individuals with asthma were further grouped according to disease severity. Severe asthma was defined as more than 10 asthmatic attacks per year. This patient group had daily medication compared to children with moderate asthma (less than 10 asthmatic attacks/yr) who took medication temporarily. Fifty-five age-matched children from the same area made up the control group. All the children were examined clinically and radiographs were taken. The results showed no statistically significant differences concerning caries prevalence in asthmatic children compared to the healthy control group. The mean sums of decayed and and filled teeth in the age group of 10 to 18 years of age were 7.8 and 6.9 in asthmatics and controls, respectively. In this study the younger asthmatic children had significantly lower secretion of paraffin-wax stimulated salivary flow rate compared to control of the same age.

Twenty-four subjects, from 10 to 20 years old, with asthma treated with β_2-agonists were matched with healthy controls of the same age, sex, and social background (Ryberg et al. 1987). Stimulated whole and parotid saliva was collected, decayed and filled tooth surfaces as well as oral hygiene habits were recorded and the sugar intake was checked. The asthmatic children had significantly lower values for secretion rate of whole saliva. The majority (70%) of the children with high Streptococcus mutans counts belonged to the asthmatic group. The concentrations of total protein and amylase in parotid saliva were significantly lower for the asthmatic children. The concentrations of other salivary constituents measured were not affected, but the secretion rate of parotid saliva was significantly lower in the asthma group. Oral hygiene and dietary habits did not differ between the groups. The asthmatic children had

higher DFS scores (14.3 in asthmatics and 10.6 in controls), but the difference was not statistically significant.

In the follow-up study on the same group (Ryberg et al. 1991) the same asthmatics and their matched controls were examined 4 years later. Samples of whole saliva stimulated by chewing and parotid saliva stimulated by citric acid were collected and dental caries was scored. In the asthmatic group the secretion rates of stimulated whole and parotid saliva were 20% and 35% lower, respectively, compared to the control group. The number of lactobacilli was higher. The asthmatic subjects had a lower output per minute of total protein, amylase, hexosamine, salivary peroxidase, lysozyme, secretory IgA, a bacteria-aggregating glycoprotein, potassium, and calcium in stimulated parotid saliva. Initial and manifest caries lesions as well as the number of DFS were significantly increased in the asthma group (17.6 and 11.9 in asthmatics and controls respectively). The authors concluded that asthmatic patients treated with $beta_2$-agonists have increased caries susceptibility due to an impaired saliva secretion caused by the use of their anti-asthmatic medication and that subjects with asthma treated with $beta_2$-agonists should receive special prophylactic attention.

In Sweden at one regional hospital all inpatients referred for a paediatric dental consultation (n = 269) were studied retrospectively during a two-year period (Arnrup et al. 1993). The children were studied regarding their medical and oral condition and subsequent dental treatment. The most frequent medical condition among the referred children was insulin dependent diabetes mellitus (20%), asthma (9%) and epilepsy (7%). Children with asthma exhibited a significantly increased caries prevalence ($p < 0.01$) compared to other chronically sick children.

McDerra et al. (1998) studied the prevalence of dental disease in British school children with asthma. A sample of 100 asthmatic children (aged 4–16 years) was examined for dental caries, periodontal condition, and tooth surface loss. School children, matched for age, sex, race and socioeconomic status were chosen for comparison. Children were divided into two age ranges; 4–10 and 11–16 years. A significant difference was found in DMFT (0.96 vs. 0.31) and DMFS (1.37 vs. 0.37) between the 4–10 year-old asthmatics children compared with healthy control children. In the 11–16 year age range, the asthmatic children had a DMFT and DMFS of 2.48 and 3.39 compared with the control children who had a DMFT and DMFS of 1.11 and 1.97 respectively. There was a significant difference in the severity and number of teeth

affected by tooth surface loss affecting labial surfaces of the anterior teeth and occlusal surfaces of the posterior teeth of asthmatic children. The investigators concluded that asthmatic children have more decay affecting their permanent teeth and more tooth surface loss than healthy controls.

The aim of the study by Kankaala et al. (1998) was to analyse the timing of first fillings posteruptively in a cohort comprising 51 asthmatic children receiving inhaled corticosteroids and living in three communities in the region of Ostrobothnia, Finland. The subjects had all been born in the 1980s and had had asthma check-ups in the local asthma clinic. A group of 102 healthy age- and sex-matched children served as controls. A longitudinal survival analysis of the timing of the first filling in the primary teeth and first permanent molars was conducted retrospectively using data from the annual dental health records. The timing of the first fillings in permanent first molars showed no statistically significant differences between asthmatic and healthy children, but the filling increments in the primary molars were consistently higher in the asthmatic group; the difference for the upper first primary molars was, for instance, statistically significant (risk ratio = 2.6; 95% confidence interval = 1.3–4.9). More extractions because of caries were also performed on primary molars in the asthmatic children. The findings support the hypothesis that factors related to the asthmatic condition may increase the risk of caries.

Meldrum et al. (2001) examined the association over time between asthma and caries increment. In a long-standing New Zealand cohort study, participants' long-term asthma histories and the 3-year net caries increment between the ages of 15 and 18 years were examined. Of the 781 who were examined at 15 and 18 years, 39 participants were consistently taking anti-asthma medication at the ages of 9, 11, 13 and 15 years (and were labelled in this study as 'medication-determined asthmatics'), 56 were identified as consistent wheezers at the ages of 9, 11, 13 and 15 years ('wheeze-determined asthmatics') and 36 were members of both groups. A smaller group (n = 9) was identified as being very-long-term asthmatics (asthma at 5 years of age and at the ages of 9, 11, 13 and 15 years). Some 206 study participants were identified as having no history of asthma, asthma medication or significant wheeze at any time up to and including of 18. The overall mean net caries increment between the ages of 15 and 18 years was 2.06 surfaces (SD, 3.76). There were no significant differences in caries increment between the 206 asthma-free participants and any of the asthma groups.

Shulman et al. (2001) explored the potential association between childhood asthma and caries using oral examination and health interview data from the Third National Health and Nutrition Examination Survey 1988–1994 (NHANES III). They found no association between the use of drugs commonly used by asthmatics (antihistamines, corticosteroids, and antiasthmatic inhalers) and df/DMF scores. Asthmatic children 4–10 years of age at all severity levels had similar dfs scores to the controls, however, severely asthmatic children 4-10 years of age had significantly lower DMFS ($p = 0.010$) and DMFT (0.049) scores than controls. Similarly, severely asthmatic children 11–16 years of age had significantly lower DMFT scores than controls ($p = 0.024$) and DMFS scores approaching statistical significance ($p = 0.053$). The study by Shulman et al. did not support the hypothesis that asthmatic children have greater caries experience than their nonasthmatic peers.

The possible effects of allergy and/or asthma on periodontal tissues has been addressed in four studies (Hyyppä et al. 1979, Bjerkeborn et al.1987, Mattson and Möller 1990, McDerra et al. 1998). In the first study report published in 1979 by Hyyppä et al. the effect of extrinsic asthma on periodontal condition was studied in a group of 30 asthmatic children (Hyyppä et al. 1979). They found that asthmatic children had more gingivitis than non-asthmatic children. The asthmatic children who received an inhaled corticosteroid as a treatment had more severe gingivitis compared with asthmatic children on disodium cromoglycate treatment. The amount of plaque was the same. A contradictory finding was reported by Bjerkeborn et al. (1987). In their study the results showed no statistically significant differences concerning gingival condition in asthmatic children compared to a healthy control group.

Mattson and Möller (1990) investigated the degree of gingival inflammation in children with rhinoconjunctivitis due to birch pollinosis. Thirty-four allergic children aged 8 to 17 years and their healthy classmates (controls) of the same age and sex were enrolled in the study. The allergic children were examined on three occasions: pollen season I, off-season and pollen season II. The controls were examined on one occasion, mixed with the allergic children at the off-season examination. The degree of gingival inflammation was studied by determining the gingival bleeding tendency by standardized probing. Absence or presence of dental plaque was recorded, and in order to compensate for differences in oral hygiene level between the participants, the bleeding/plaque ratio was calculated. The comparisons of the bleeding/plaque ratios revealed statistically significantly higher mean ratios in the allergic children during

pollen seasons compared with off-season and with the controls. The results indicate that during the pollen season, children with allergic rhinoconjunctivitis exhibit an enhanced degree of gingival inflammatory reaction.

In the study by MacDerra et al. (1998) asthmatic children had significantly more plaque, gingivitis and calculus compared with the control group. The investigators concluded that asthmatic children have poorer periodontal status than the healthy controls.

The effects of asthma and allergy on TMJ disorders has not been widely studied and the major information is related to the differences in jaw morphology and in occlusion found between asthmatics/ allergic and healthy children. The relationships between malocclusion and atopic diseases and other common predisposing factors were studied clinically and biometrically in a nonselected cohort of 217 7 year-old children (Hannuksela and Väänänen 1987). Normal Class I occlusion was more common in children with atopic respiratory symptoms than in nonatopic children. Posterior crossbites were found in children with atopic dermatitis, those with frequent infections, and in those sucking their fingers or a dummy beyond the age of 4 years more often than in other children. The results of Hannuksela and Väätäinen provide support for the view that atopic hyperreactivity is a predisposing factor for posterior crossbites.

Venetikidou (1993) examined the relationship of a compromised airway i.e. mouth breathing in asthmatic children, and the effect that the airway compromise has on occlusal and facial characteristics. The study consisted of sixty-four children of both sexes, ranging in age from 3 to 16 years. Thirty-two subjects were from the pulmonary and allergy clinic of the Floating Hospital, New England Medical Center, who were present for follow-up and/or treatment of asthma. Thirty-two randomly selected children were selected from the paediatric clinic in Tufts University School of Dental Medicine to serve as controls. The two groups were matched for age, sex and race. A statistically significant difference was found between the groups in frequency of crossbites and frequency of mouth breathing. Additionally, a statistically significant relationship was found between the frequency of crossbites and the facial type in the experimental group. The frequency of crossbites appears to be related to abnormal facial types.

Little attention has been paid to the possible effects of inhaled asthma medication on the oral cavity. From the inhaled dose only about 10–15% reaches the lungs and nearly 80% is deposited in the mouth and/or orophanryngeal area from which it will consequently be swallowed (Lipworth 1995). The usual local side effects of inhaled

corticosteroids are hoarseness (dysphonia), oropharyngeal candidiasis, and throat irritation and cough (Milne and Grompton 1974, Shaw and Edmunds 1986, Toogood 1990, Barnes and Pedersen 1993). To decrease the risk of local side effects, the patients are usually advised to rinse their mouths after drug intake.

Rydberg et al. reported decreased salivary flow rate in asthmatics and also changes in salivary composition (Rydberg et al. 1991) and linked it to the use of inhaled β_2-agonists (Rydberg et al. 1990). The effects of inhaled asthma medication on plaque pH have been addressed in the study by Kargul et al. (1998). They investigated the effect on saliva and plaque pH of inhaled β_2 agonist (salbutamol) and inhaled corticosteroid (fluticasone propionate) in 30 asthmatic children. Both medications were administered from a pMDI via spacer device. Interdental pH values were measured at baseline and 1, 5, 10, 20, and 30 minutes after the inhalation of medications. The authors found a decrease in both salivary and interdental plaque pH 30 minutes after the inhalation of both salbutamol and fluticasone. However, conclusive evidence requires a longitudinal follow-up of asthmatic subjects who start using these medications.

Taken together the published reports give a somewhat contradictory picture of the association between asthma and dental caries. The discrepancies between the different publications can be explained by different study populations, changes in caries prevalence over time, methodological differences, and differences in used asthma medications. Some of the older studies are based on a rather small number of subjects included in the study (Hyyppä and Paunio 1979, Bjerkeborn et al. 1987, Ryberg et al. 1987, Ryberg et al. 1991). Some of the studies are retrospective in nature (Storhaug 1985, Arnrup et al. 1993, Meldrum et al. 2001, Shulman et al. 2001) and most of the studies were cross-sectional in design.

A methodological concern arises from the natural history of dental caries. Although it is widespread and common, there has been a marked decline in the prevalence of caries in children in industrialised countries during the past twenty years. At the same time it is polarized, so that there are usually some small high-risk groups of children having a lot of caries while the major part of the same age group is nearly disease-free (Vehkalahti et al. 1997). Calculation of the mean DMFS or DMFT values leads to very low mean values, but because of the presence of these small high-risk groups the variation is wide, which leads to wide confidence intervals. This was also evident in the studies by Meldrum et al. and Shulman et al. In the study by Meldrum et al. the reported net caries increment from 15 to 18 years of age varied from 2.13 to 3.00,

while the standard deviation varied from 3.68 to 4.80, indicating a substantial variation in the outcome variable. In the study by Shulman et al. the researchers were bound to make adjustments to the DMFS scores because of the large percentage of subjects with DMFS being 0. Under these circumstances conventional hypothesis-testing may not be a relevant way of analysing the results, and a different epidemiological approach may be required.

The evidence for the association of other oral diseases and asthma is derived from several small-scale studies and the major concern is the small number of subjects studied. Moreover, the reports indicating an increased risk for oral diseases in asthmatics compared to non-asthmatic subjects are mainly obtained from studies in children, adolescents and young adults. The information about the oral health in asthmatic adults is still lacking.

3 Aims of the study

1. The primary aim is to study the association between allergic and non-allergic asthma, and oral diseases and the following selected symptoms of oral diseases: dryness of mouth (xerostomia), sore mouth, feeling of foul taste (halitosis), TMJ disorders (pain, stiffness, clicking), toothache, sensitivity to hot, cold or sweet, and bleeding from gums (gingival bleeding).
2. The secondary aim of the study is to refine the exposure due to asthma in contrast to a general atopic tendency (presence of self-reported allergy) or exposure due to asthma medication by estimating the combined effects of these three exposures and the selected symptoms of oral diseases.

The research project consists of two separate studies:

1. Pilot Study. The Pilot Study investigated the oral health status, stimulated salivary flow rate and saliva composition in a group of adult asthmatic and non-asthmatic subjects. Part of the results from the Pilot Study has been published in two papers (Laurikainen and Kuusisto 1998, Lenander-Lumikari et al. 1998).
2. Questionnaire Survey. A population-based, cross-sectional study compared the prevalence of self-reported symptoms of the following oral diseases between adult asthmatic and non-asthmatic subjects: dry mouth, sore mouth, foul taste (halitosis), temporo-mandibular joint (TMJ) disorders (pain, stiffness, clicking), toothache, sensitivity to hot, cold or sweet, and bleeding from gums.

4 Material and methods

4.1 Populations

In the Pilot Study the asthmatic subjects (n = 37) were enrolled from among patients visiting the Clinic of Pulmonary Diseases, Tampere University Hospital (TAUH), Consecutive asthmatic patients visiting the clinic were informed about the study and if they fulfilled the entry criteria, informed consent for participation in the study was requested. The non-asthmatic subjects were enrolled from among subjects who visited the Occupational Health Care Center of Tampere for regular check-ups (n = 29) and from among students at the University of Tampere who were visiting the Student Health Care Foundation Clinic for regular check-ups (n = 6). For each asthmatic patient recruited in the study an age and gender matched counterpart was enrolled from the consecutive subjects visiting Occupational Health Care Center or Student Health Care Foundation Clinic. All asthmatic subjects and controls included in this study were sampled from Tampere Region. This region has a total population of around 430 000 inhabitants. Of the 37 asthmatics eligible for the Pilot Study, 33 (24 female, 9 male) were included in the statistical analyses. Four were excluded because of lack of a suitable counterpart.

In the Questionnaire Survey the registers from the Social Insurance Institution (KELA) were used as the sampling base. A random sample of 1000 adult asthmatics entitled to special reimbursement for anti-asthmatic medications was drawn from the Drug Register of KELA which includes all Finnish citizens. In the same way a random sample of 1000 adult non-asthmatic subjects (healthy) was drawn from the register. Common entry criteria to the Questionnaire Survey were age 20–55 years, and living in the predefined geographical area of Tampere Region.

KELA's register of subjects entitled to special reimbursement for anti-asthmatic medications contains both asthmatics and subjects using anti-asthmatic medicines for the treatment of other obstructive lung diseases, mainly chronic obstructive pulmonary disease (COPD). The presence of asthma was confirmed by asking the participating subjects if they had asthma. The subjects were then allocated into two groups, asthmatics and healthy subjects, on the basis of answers to question 32 in Appendix 1 (“Do you have any of the following diseases or symptoms? Only diseases diagnosed by

a physician should be recorded"). If the subject answered "yes" for asthma she/he was classified as an asthmatic. Those who answered "no" were classified as healthy and they served as a control group. It should be noted that in this context, "healthy" refers to a non-asthmatic subject. This procedure also re-grouped correctly the possible asthmatics in the control group who had newly detected asthma but were not yet included in the KELA register.

Of the 2000 subjects included in the Questionnaire Survey, 1216 (60.8%) returned the questionnaire after the first mailing round. After the second mailing round the total number of respondents was 1234 (61.7%), including 626 asthmatics and 608 controls. Of those who returned the questionnaires, 15 subjects among the asthmatics and 2 subjects among the controls did not meet the inclusion criteria, and were excluded from the statistical evaluation. The reason for exclusion was that the age of the subject was not within the predefined range (from 20 to 55 years). The final sample size was 1217 subjects (611 asthmatics and 606 controls).

4.2 Assessments

4.2.1 Pilot study

Clinical assessments

Oral examinations were carried out according to the WHO guidelines (WHO 1987). The examinations were performed in a dentist's chair, under a good light using a plane mouth mirror, an explorer and a periodontal probe. The following items were recorded:

- Decayed, missing and filled teeth (DMFT)
- Periodontal status. Periodontal status was recorded using a similar scoring system as in the CPITN-index (WHO 1987). In this study a score ranging from 0 to 4 was given to every tooth.
- Occlusion
- Condition of oral mucous membranes (cheeks, tongue)
- Lips

The oral examination was performed by one person according in an unmasked manner. Thus during the examination the examiner was aware if the subject was asthmatic or not.

Collection and treatment of saliva samples

Collection and treatment of saliva samples were performed according to the standardised protocol (Tenovuo 1995). Paraffin-stimulated whole saliva was collected in chilled graduated glass tubes between 8.00 and 10.00 in the morning. Saliva was collected for five minutes from all the participants and the collected volumes were measured. The participants were not allowed to use any drugs for one hour before saliva collection and they were also asked to refrain from smoking, eating and drinking for 1 hour before collection. Immediately after the collection 100 µl of uncentrifuged saliva was transferred to a plastic tube containing fresh tryptic soy broth (TSB, Oxoid, Basingstoke, United Kingdom) supplemented with 20% glycerol (used for micro-biological analysis). The samples were stored frozen at –20° C for 1 month prior to bacterial cultivation. Another portion of 50 µl of uncentrifuged saliva was separated and transferred to Eppendorf vials (Plastic Trade, Helsinki, Finland) for the analysis of lactoferrin and calcium (Ca^{2+}) concentrations and lysozyme activity. The tubes were frozen at –20° C before analysis.

In the chemical and microbiological assays the following items were analysed from the saliva samples:

- Total protein
- Myeloperoxidase
- Salivary peroxidase
- Lactoferrin
- Lysozyme
- Calcium
- Potassium
- Sodium
- Mutans streptococci
- Lactobacilli
- Candida
- Total anaerobic flora

The details of the chemical assays have been described previously by Lenander-Lumikari et al. (1998). Briefly, the total protein concentration was measured by the method of Lowry et al. (1951) with bovine serum albumin (Sigma Chemical Co, St. Louis, MO) as a standard. Salivary peroxidase and myeloperoxidase were analysed according to the method developed by Vilja et al. (1991). The lactoferrin concentrations were determined by an immunometric assay using biotinylated antibody and avidin-biotin-peroxidase complex (Vilja et al. 1985). The immunometric assay for lysozyme

was similar to the lactoferrin assay. Before the cultivation of salivary microbes the tubes with tryptic soy broth were thawed and vortexed thoroughly for 1 minute. After serial-fold dilutions the bacteria were plated as follows: Mutans streptococci on mitis salivarius bacitracin agar plates, lactobacilli were cultivated on Rogosa SL agar plates and candida on Sabouraud agar plates. The total anaerobic flora was determined by palting samples on blood agarplates containing 5% sheep blood and incubating anaerobically for two days.

Formation of new variables

DMFT was calculated for each subject according to Klein and Palmer (1940). Individual periodontal status was expressed by a periodontal status index (PSI) obtained by dividing the number teeth with inflamed periodontal tissues (CPITN score equal to 1 or more) by the number of all remaining teeth; the quotient is expressed as a percentage. The frequency of sugar intake was estimated by a sugar consumption index (SCI). The SCI was constructed as follows: The frequency of use of sugar, soft drinks and sweet pastries was estimated in the questionnaire by a score ranging from 0 to 4; 0 = never; 1 = once weekly or less; 2 = 2-6 times weekly; 3 = once or twice daily, and 4 = more than twice daily. For the calculation of SCI these scores were summed. The highest possible value for SCI was 24.

The subjects also recorded the frequency of tooth brushing on a scale similar to that used for sugar consumption. The use of toothpicks, dental floss and mouthwashes containing fluoride was estimated on a scale ranging from 0 to 3; 0 = never; 1 = irregularly; 2 = regularly weekly; 3 = regularly daily. In addition to that, a score measuring the use of dental services (range from 0 to 3) and the use of toothpaste containing fluoride (range 0 to 2) were entered in the questionnaire. An oral hygiene index (OHI) was calculated as a sum of these scores related to the oral hygiene habits. The highest possible value for OHI was 18.

The data from the analysis of saliva samples are expressed in three different ways: as crude concentrations, as salivary output (concentration x salivary flow rate), and as relative concentrations (amount / secreted protein). One subject in the asthmatic group had extremely high concentrations of myeloperoxidase and was considered an outlier. This participant was excluded from the statistical analyses in Tables 6, 7, and 8.

Statistical analyses in the Pilot Study

The mean value and standard deviation (SD) were calculated for each variable measured on an interval scale. The statistical significance of the differences between the groups in SSFR, salivary pH, DMF and PSI was tested by analysis of covariance. In the model, the length of basic education was fitted as covariate. The statistical significance of the differences between the groups in SCI and in OHI was tested with the Wilcoxon rank sum test. Moreover, 95% confidence intervals (95% CI) for the differences between the adjusted means of SSFR, salivary pH, DMF, and PSI were calculated.

The statistical significance of the differences between the groups in salivary parameters was tested with Student´s *t*-test for unpaired samples. Moreover, 95% CIs for the differences between the means were calculated. All computations except 95% CIs were performed with BMDP Statistical Package, version 1990. The 95% CIs were calculated with Confidence Interval Analysis (CIA) program running in PC. In the statistical tests a two-sided p-value of 0.05 was considered statistically significant.

4.2.2 Questionnaire Survey

Collection of data

A questionnaire (Appendix 1) was first mailed in December 1995 and to non-respondents again in March 1996. The questionnaire dealt with the following items:

- Background information (age, gender, basic education, professional education, place of residence, smoking history, frequency of alcohol intake)
- Information on dietary habits (sugar intake, special diets, use of vegetables)
- Information on oral health care habits
- General health and use of any medications
- Use of removable dental prostheses
- Difficulties in chewing food
- Symptoms for oral diseases.

In the questionnaire the presence or absence of the following symptoms of oral diseases were evaluated:

- Dryness of mouth (xerostomia)
- Sore mouth
- Feeling of foul taste (halitosis)
- TMJ disorders (pain, stiffness, clicking)
- Toothache
- Sensitivity to hot, cold or sweet
- Bleeding from gums (gingival bleeding).

Calculation of indices

The frequency of sugar intake was estimated in a similar manner as in the Pilot Study and the SCI was also constructed in the same way. The highest possible value for SCI was 24. Oral hygiene habits were also measured with an identical system as in the Pilot Study, and OHI was calculated accordingly. The highest possible value for OHI was 18.

Statistical methods

The statistical significance of the difference between the groups in SCI and in OHI was tested with Wilcoxon rank sum test. Statistical significance of the differences between the groups in categorical variables (gender, place of residence, smoking, frequency of alcohol intake, basic education and professional education, self-reported health status, use of removable dentures and difficulties in mastication) were tested with Pearson chi-square test.

The effect of risk factors (asthma, allergy and asthma medication) on the occurrence of symptoms of oral diseases was analysed as follows: In the first phase the number of asthmatics and controls reporting symptoms was tabulated. Then crude ORs and 95% CIs for crude ORs were calculated in order to estimate the odds of having symptoms among asthmatics compared to healthy subjects. Finally, adjusted ORs and 95% CIs were calculated by using logistic regression. Adjustment was made for age, gender, smoking, frequency of alcohol intake, place of residence, education, professional education, and the concomitant use of medication other than for asthma. The study population was also grouped according to the presence of self-reported allergy (allergic and non-allergic group) and according to the use of asthma medication (users and non-users). The groups were analysed in a similar manner as asthmatics and healthy subjects.

Because asthma, like oral diseases, has several factors that affect its severity and occurrence, other causes than asthma may in fact account for the association between asthma and oral health. In order to estimate the potential confounding effect of age, gender, smoking, frequency of alcohol intake, place of residence, education, professional education and the concomitant use of medication other than for asthma, the following approach was used: The effects of these variables on the occurrence of asthma were analyzed by calculating both crude and adjusted ORs and 95% CIs for adjusted ORs. In calculating the adjusted ORs, all the variables considered to be potential confounders were included in the model at the same time. Then the effects of potential confounding variables on the occurrence of symptoms of oral diseases were analysed as follows: In the first phase crude ORs were calculated. In the second phase

logistic regression analysis was employed to calculate adjusted OR for the occurrence of symptoms. In the calculation of adjusted ORs, all potential confounders were kept in the model at the same time. The summary of factors considered to be possible confounding factors is given in Table 2.

For the evaluation of the effects of asthma, allergy and asthma medication separately, a new variable ("Asthma") was formed from these three variables. This new variable had eight classes and included all possible combinations of these three variables. The description of the new variable is given in the Table 3. The effects of "Asthma" on the occurrence of symptoms of oral diseases were studied in the same way as the effects of potential confounders. In all computations BMDP Statistical Package, version 1990 was used.

Table 2. Summary of the variables considered as potential confounding factors in the Questionnaire Survey.

Factor	Number of classes	Description of factor
Age	2	Subject were allocated into two groups, younger and older. The cut-off point was 35 years of age.
Gender	2	The classes included females and males
Smoking	3	The subjects were allocated into three classes according to the smoking habits. The classes were: current smokers; ex-smokers (had stopped smoking before the study); and life-long non-smokers.
Frequency of alcohol intake	3	The subjects were allocated into three classes according to the frequency of alcohol intake. The classes were: never (= abstainer); moderate (= 1-4 times a month); and high (= more than 4 times a month).
Place of residence	2	The subjects were grouped according to their living environment into two classes: urban (= living in town or in village centre); and rural (= living in a remote rural area).
Basic education	3	The subjects were allocated into three classes according to the length of their basic education. The classes were: less than 9 years; 9 years; and 12 years.
Professional education	2	The subjects were allocated into two classes according to theit level of professional education. The classes were: lower (=unskilled and semi-skilled workers, skilled workers); higher = (lower and upper white collar workers, university graduates and students).
Concomitant use of medication other than for asthma	2	The subjects were allocated into two classes according to the use of medication other than for asthma. The classes were users and non-users.

Table 3. Allocation of subjects in the Questionnaire Survey to different groups according to presence of asthma (As), allergy (Al) and asthma medication (Me). The number of subjects (N) in each group is also given.

Group	As	Al	Me	N	Description of group
0	–	–	–	486	Subjects without asthma, allergy and asthma medication (Healthy).
1	+	–	–	61	Subjects with asthma, but without allergy and asthma medication
2	–	+	–	107	Subjects without asthma and asthma medication, but having allergy
3	–	–	+	5	Subjects without asthma and allergy, but with asthma medication
4	+	+	–	126	Subject with asthma and allergy, but without asthma medication
5	–	+	+	3	Subjects without asthma, but with allergy and asthma medication
6	+	–	+	173	Subjects with asthma and asthma medication, but without allergy
7	+	+	+	249	Subjects with asthma, allergy and asthma medication.

The size of the Groups 3 and 5 was extremely small – only 5 and 3 subjects respectively. Because these groups could include subjects other than asthmatics, or subjects in whom the asthma diagnosis was not yet confirmed, these groups were excluded from the final reporting of both crude and adjusted ORs.

5 Results

5.1 Results from the Pilot Study

5.1.1 Subject characteristics

The mean (SD) age was 36.0 (7.4) years in asthmatics and 36.5 (7.1) in healthy subjects. The mean duration of asthma was 5 years, ranging from less than one year to 24 years. Sixteen asthmatics (48.5%) had had diagnosed asthma for one year or less. In five asthmatics the disease was graded mild, in 22 asthmatics as moderate and 6 asthmatics were classified as severe asthmatics. Twenty-one subjects (64%) in the asthma group were atopic.

In general the subjects visited dentists regularly and the median time from the last visit was one year for both groups. The frequency of sugar intake was higher among controls than among asthmatics. The median SCI was 5 in the asthma group compared to 7 in the control group; this difference was statistically significant ($p = 0.009$, Wilcoxon rank sum test). Concerning oral hygiene habits, there was also a statistically significant difference between the groups in OHI ($p = 0.007$, Wilcoxon rank sum test): the medians were 7 and 8 in the asthmatics and controls respectively

Major differences between the groups were found in basic education and professional education, and there were also some differences in smoking habits and in the frequency of alcohol intake (Table 4). Concerning smoking, however, in both groups the majority of the subjects (58%) were lifelong non-smokers, while 42% were either current or ex-smokers. In terms of frequency of alcohol intake the same percentage (12%) were frequent users, and the vast majority (73% and 85% in asthmatics and healthy subjects respectively) were moderate users.

Table 4. Numbers (n) and percentages (%) of subjects in different categories of basic education, professional education, smoking and alcohol consumption in the Pilot Study (Laurikainen and Kuusisto 1998).

	Asthmatics (n=33)		Healthy (n=33)	
	n	%	n	%
Basic education				
– 6 years or less	10	30	5	15
– 9 years	9	30	3	9
– 12 years	14	40	25	76
Professional education				
– Semi- or unskilled	13	39	6	18
– Skilled workers	6	19	2	6
– Lower white collar	13	39	15	46
– Upper white collar / academic	1	3	10	30
Smoking				
– Lifelong non-smoker	19	58	19	58
– Stopped smoking	4	12	9	27
– Current smoker	10	30	5	15
Frequency of alcohol intake				
– Never	5	15	1	3
– Once monthly or less	13	40	10	30
– 2–4/month	11	33	18	55
– 2–3/week or more	4	12	4	12

5.1.2 Clinical findings

A statistically significant difference was found in the amount of periodontal inflammation and in the stimulated salivary flow rate between the groups (Table 5). A small but insignificant difference in the DMFT values was observed between the groups. The mean (SD) crude DMFT score was 20.1 (5.8) in asthmatics and 18.4 (7.6) in healthy subjects.

Table 5. Adjusted mean (SD) of stimulated salivary flow rate (SSFR); salivary pH; sum of decayed, missing and filled teeth (DMFT); and periodontal status index (PSI) and 95% confidence interval (95%CI) for differences between the means in Pilot Study (modified from Laurikainen and Kuusisto 1998).

	Asthmatics	Healthy	Difference	95% CI
PSI (%)	50.3 (23.7)	39.4 (20.4)	10.9	0.9–20.9
SSFR (ml/min)	1.0 (0.5)	1.3 (0.5)	– 0.3	–0.6–0.0
Salivary pH	7.9 (0.4)	8.1 (0.4)	– 0.2	–0.4–0.0
DMFT	19.3 (5.8)	18.9 (7.3)	– 0.4	–2.2–3.0

Eighteen asthmatic subjects had at least one decayed tooth, compared to sixteen in healthy subjects. When the subjects having two or more decayed teeth were taken into account, the numbers were 9 and 2 in asthmatics and controls respectively. Mucosal lesions in the oral cavity were found in 15 asthmatics (45%) and in eight controls (24%).

5.1.3 Saliva analysis

In the same study the concentrations of total protein, lactoferrin, lysozyme, myeloperoxidase, salivary peroxidase, calcium (Ca^{2+}), potassium (K^{+}), sodium (Na^{+}) and thiocyanate (SCN^{-}) in whole saliva of 26 adult asthma patients were compared with those of 33 non-asthmatic controls. The saliva was also analysed for mutans streptococci, lactobacilli, total anaerobic flora and Candida species. The only statistically significant difference between the groups was found in the mean crude concentration of myeloperoxidase (Table 6).

Table 6. Mean (SD) crude concentrations of selected proteins and electrolytes in paraffin-stimulated whole saliva of asthmatics and control subjects and their 95% confidence intervals (95% CI) (modified from Lenander-Lumikari et al. 1998).

	Asthmatics (n = 26)	Healthy (n = 33)	Difference	95% CI of the difference
Total protein (mg/ml)	1.265 (0.416)	1.135 (0.225)	0.13	–0.40 – 0.30
Lactoferrin (µg/ml)	3.48 (1.09)	3.33 (0.95)	0.15	–0.38 – 0.68
Lysozyme (µg/ml)	1.04 (0.94)	1.39 (1.37)	–0.35	–0.98 – 0.28
Myeloperoxidase * (ng/ml)	164.4 (136.5)	95.2 (110.0)	69.5	4.4 – 134.0
Salivary peroxidase (ng/ml)	369.6 (119.5)	371.8 (92.3)	–2.2	–57.4 – 53.0
Calcium (mM)	1.22 (0.23)	1.27 (0.18)	–0.05	–0.16 – 0.06
Potassium (mM)	15.47 (2.68)	14.36 (2.33)	1.11	–0.20 – 2.42
Sodium (mM)	11.78 (5.58)	13.03 (7.19)	–1.25	–4.68 – 2.18

* One subject excluded

In general the mean output (salivary flow rate x concentration) of the measured parameters was higher in the controls than in the asthmatics except for myeloperoxidase, but the difference was statistically significant only for Ca^{2+} (Table 7).

Table 7. Mean (SD) outputs (stimulated salivary flow rate x concentration) of selected proteins and electrolytes in whole saliva in asthmatics and controls and their 95% confidence intervals (95% CI).

	Asthmatics (n = 26)	Healthy (n = 33)	Difference	95% CI of the difference
Total protein (mg/min)	1.31 (0.87)	1.48 (0.64)	–0.17	–0.56 – 0.22
Lactoferrin (µg/min)	3.47 (2.04)	4.30 (2.06)	–0.83	–1.91 – 0.25
Lysozyme (µg/min)	1.01 (0.91)	2.03 (3.12)	–1.02	–2.29 – 0.25
Myeloperoxidase * (ng/min)	155.9 (145.4)	129.5 (155.9)	26.4	–53.6 – 106.0
Salivary peroxidase (ng/min)	387.1(236.0)	488.5 (236.1)	–161.4	–225.0 – 22.6
Calcium (µg/min)	50.2 (30.3)	67.8 (31.8)*	–17.6	–34.0 – –1.24
Potassium (µg/min)	596.6 (296.6)	731.0 (287.0)	–134.4	–287.0 – 18.5
Sodium (µg/min)	307.8 (269.2)	428.2 (381.6)	–120.4	–297.0 – 56.5

* One subject excluded.

The relative amounts (protein/total protein content) of lysozyme and salivary peroxidase were higher in controls than in asthmatics but the differences were not significant (Table 8).

Table 8. Mean (SD) relative concentrations and their 95% confidence intervals (95% CI) in lactoferrin, lysozyme, myeloperoxidase, and salivary peroxidase in saliva in asthmatics and controls. The values represent the relative proportion of secreted protein / total salivary protein.

	Asthmatics (n = 26)	Healthy (n = 33)	Difference	95% CI of the difference
Lactoferrin (µg/mg protein)	2.96 (1.04)	2.97 (0.77)	–0.01	–0.48 – 0.46
Lysozyme (µg/mg protein)	0.96 (0.99)	1.27 (1.35)	–0.31	–0.94 – 0.32
Myeloperoxidase * (ng/min)	126.5 (102.0)	86.6 (98.2)	39.9	–12.5 – 92.3
Salivary peroxidase (ng/mg protein)	300.8 (65.8)	329.8 (66.1)	–29.0	–63.6 – 5.64

* One subject excluded.

No differences between the groups were found in microbial counts (Table 9).

Table 9. Mean (SD) amounts (log c.f.u.) and 95% confidence intervals (95% CI) for the difference between means of Mutans streptococci, total anaerobic flora, lactobacilli flora and Candida species found in whole saliva of asthmatics and controls in the Pilot Study.

	Asthmatics (n = 25)	Healthy (n = 32)	Difference	95% CI of the difference
Streptococcus mutans	4.56 (0.74)	4.46 (0.69)	0.10	–0.30 – 0.52
Total anaerobic flora	7.78 (0.57)	7.64 (0.47)	0.14	–0.15 – 0.43
Lactobacilli flora	2.69 (2.08)	2.43 (1.98))	0.26	–0.90 – 1.42
Candida –species	2.28 (1.76)	2.68 (1.63)	-0.40	–1.36 – 0.56

5.2 Results from the Questionnaire Survey

5.2.1 Patient demographics and background information

The mean (SD) age of the respondents was 40 (10) years among asthmatics and 38 (9) years among controls. The percentages of females were 62% and 56% respectively. The differences in age and gender distribution were not statistically significant. In asthmatics 422 (69%) of subjects used asthma medications and the corresponding number in controls was 8 (1%). Medication other than for asthma were used by 236 (39%) of asthmatics while in controls 85 (14%) used other medications. Seven subjects had incomplete data about the use of medications. The percentages of subjects reporting allergy were 62% in asthmatics and 19% in controls.

5.2.2 Use of sugar, other dietary habits and oral hygiene habits

No difference between the groups was observed in frequency of sugar intake, or in frequency of the use of fresh vegetables. The median SCI was 6 in both asthmatics and healthy subjects. In the use of special diets there was a significant difference between the groups. In healthy subjects 10% had a special diet compared to 29% in asthmatics ($p<0.01$, Pearson chi-square test). The most common diet was lactose-free diet (13% in asthmatics and 5% in healthy). The oral hygiene habits were broadly similar in the

groups, and the OHI was on the same level in both groups; the median score was 8 for both asthmatics and healthy subjects. In both groups the vast majority visited the dentist regularly and the median time since the last visit was one year.

5.2.3 Use of removable dentures and problems in chewing food

The use of full dentures in both upper and lower jaw was statistically significantly more common among asthmatics: 3 % of asthmatics and 1 % of healthy had full dentures ($p = 0.012$, Pearson chi-square test), but the overall prevalence of full denture usage was low. No differences between asthmatics and non-asthmatics were found in the use of any type of removable dentures. In asthmatics 12% of the group had some kind of removable denture while the corresponding figure in healthy subjects was 10%. In chewing food 92% of healthy subjects did not have any problems while the corresponding percentage in asthmatics was 82% ($p<0.01$, Pearson chi-square test). The percentage of subjects having problems with mastication was 3% in healthy subjects and 10% in asthmatics. However, the percentages of subjects who could not give an opinion were 4% and 8% respectively.

5.2.4 Symptoms of oral diseases and asthma, allergy and asthma medication

More asthmatic than healthy subjects reported symptoms of oral diseases. The probability of having dry mouth, sore mouth, halitosis and also symptoms of TMJ disorders was significantly higher among asthmatics than among healthy subjects. The differences persisted even after adjustment for the potential confounding variables: age, gender, smoking, frequency of alcohol intake, place of residence, education, professional education, and the concomitant use of medication other than for asthma (Table 10).

Table 10. Number (n) and percentage (%) of subjects reporting symptoms of oral diseases among asthmatic (Asthma, n = 611) and non-asthmatic subjects (Healthy, n = 606), crude and adjusted odds ratios (OR) and 95% confidence intervals for both ORs (95% CI).

Symptom	Subjects with symptoms				Crude		Adjusted	
	Asthma		Healthy		OR	95% CI	OR	95% CI
	n	%	n	%				
Dry mouth	144	24	76	12	2.2	1.6 – 2.9	1.5	1.1 – 2.1
Sore mouth	74	12	39	6	2.0	1.3 – 3.0	1.7	1.1 – 2.6
Halitosis	202	33	142	23	1.6	1.2 – 2.1	1.6	1.2 – 2.1
TMJ Pain	55	9	16	3	3.6	2.1 – 6.4	2.7	1.5 – 4.9
TMJ Stiffness	46	8	18	3	2.7	1.5 – 4.6	2.2	1.2 – 4.0
TMJ Clicking	98	16	67	11	1.5	1.1 – 2.2	1.4	1.0 – 2.0
Toothache	62	10	49	8	1.3	0.9 – 1.9	1.2	0.8 – 1.8
Sensitivity	208	34	181	30	1.2	1.0 – 1.5	1.1	0.9 – 1.4
Bleeding	228	37	206	34	1.2	0.9 – 1.5	1.1	0.9 – 1.4

When the data from the study population were analysed according to the presence of self-reported allergy, allergic subjects reported more symptoms of oral diseases than non-allergic subjects. (Table 11). Allergic subjects had significantly higher probability of having symptoms of TMJ disorders, sore mouth, bleeding from gums, halitosis and dry mouth. Again, the results remained nearly similar after adjustment.

Table 11. Number (n) and percentage (%) of subjects reporting symptoms of oral diseases among allergic (Allergy, n = 489) and non-allergic subjects (No allergy, n = 728) and crude odds ratios (OR) and 95% confidence intervals for crude OR (95% CI).

Symptom	Subjects with symptoms				Crude		Adjusted	
	Allergy		No allergy		OR	95% CI	OR	95% CI
	n	%	n	%				
Dry mouth	103	21	117	16	1.4	1.0 – 1.9	1.2	0.9 – 1.7
Sore mouth	58	12	55	8	1.6	1.1 – 2.4	1.7	1.1 – 2.6
Halitosis	164	34	180	25	1.5	1.2 – 2.0	1.5	1.1 – 1.9
TMJ Pain	50	10	21	3	3.8	2.3 – 6.5	3.1	1.8 – 5.3
TMJ Stiffness	34	7	30	4	1.7	1.0 – 2.9	1.4	0.8 – 2.5
TMJ Clicking	91	19	74	10	2.0	1.4 – 2.8	1.9	1.4 – 2.7
Toothache	48	10	63	9	1.2	0.8 – 1.7	1.1	0.7 – 1.7
Sensitivity	173	35	216	30	1.3	1.0 – 1.7	1.2	0.9 – 1.5
Bleeding	207	43	227	31	1.6	1.3 – 2.1	1.6	1.2 – 2.0

Table 12. Number (n) and percentage (%) of subjects reporting symptoms of oral diseases among subjects with anti-asthma medication (Medication, n = 433) and without anti-asthma medication (No medication, n = 777) and crude odds ratios (OR) and 95% confidence intervals for crude OR (95% CI).

Symptom	Subjects with symptoms				Crude		Adjusted	
	Medication		No medication		OR	95% CI	OR	95% CI
	n	%	n	%				
Dry mouth	124	29	95	12	2.9	2.1 – 3.9	2.0	1.4 – 2.7
Sore mouth	59	14	52	7	2.2	1.5 – 3.3	1.6	1.0 – 2.5
Halitosis	146	34	194	25	1.5	1.2 – 2.0	1.5	1.1 – 1.9
TMJ Pain	43	10	28	4	2.9	1.8 – 4.8	2.0	1.2 – 3.4
TMJ Stiffness	37	8	27	4	2.6	1.6 – 4.3	2.0	1.1 – 3.4
TMJ Clicking	70	16	95	12	1.4	1.0 – 1.9	1.2	0.8 – 1.7
Toothache	45	10	65	8	1.3	0.8 – 1.9	1.2	0.7 – 1.8
Sensitivity	143	33	244	31	1.1	0.8 – 1.4	0.9	0.7 – 1.2
Bleeding	153	35	278	36	1.0	0.8 – 1.3	1.0	0.7 – 1.3

The data from the study population were also analysed according to the use of asthma medication (Table 12). In this analysis those who used asthma medications had higher probabilities of having symptoms of dry mouth, sore mouth, halitosis, and TMJ disorders. The probabilities of having toothache, sensitivity or bleeding from gums were on the same level in both groups.

In summary, from the risk factors studied asthma and use of asthma medication were associated with increased probability of having dry mouth, halitosis, and pain and stiffness in TMJ. Self-reported allergy was associated with higher probability of sore mouth, halitosis, pain and clicking in TMJ area and gingival bleeding.

5.2.5 Evaluation of the role of potential confounding variables

Detailed results of the evaluation of the role of potential confounding variables on the occurrence of asthma and occurrence of symptoms of oral diseases are shown in Tables 1.2–10.2 in Appendix 2. The summary of the effects is shown in Table 13. Except for the use of medication other than for asthma, the factors that were considered to be potential confounding factors (age, gender, smoking, frequency of alcohol intake, residence, education, professional education and concomitant use of medication other than for asthma) had mainly a slight effect on the probability of having asthma.

Table 13.Summary of effects of factors considered to be potential confounders. Scoring of the effect was as follows: If the adjusted OR was greater than 0.8 or smaller than 1.2 there was no effect (-). If the adjusted OR ranged from 0.5 to 0.8 or from 1.2 to 2.0 the effect was considered slight (+). If the adjusted OR was smaller than 0.5 or greater than 2.0 the effect was considered marked (++).

Potential confounder	Asthma	Dry mouth	Sore mouth	Halitosis	Pain in TMJ	Stiffness in TMJ	Clicking in TMJ	toothache	Sensitivity	Bleeding
Age	–	+	+	+	–	+	–	–	+	+
Gender	+	-	–	–	–	+	–	+	+	+
Smoking	+	+	+	+	+	+	–	+	+	+
Frequency of alcohol intake	+	–	+	+	++	+	+	+	+	+
Place of residence	+	–	+	–	–	+	+	+	–	-
Basic education	+	+	+	+	+	+	+	+	+	+
Professional education	+	+	+	+	–	+	–	+	+	+
Use of medication other than for asthma	++	++	+	–	++	++	+	+	+	-

Subjects who used medication other than for asthma had significantly higher probability for having asthma compared to non-users (Table 1.2). Among males the probability of having asthma was somewhat lower compared to females. Among current smokers the probability of asthma was on the same level as among non-smokers, but among those who had stopped smoking there were more asthmatics than among non-smokers. Frequency of alcohol use and residence had a modest effect on the probability of having asthma, as well as basic education and professional education. There was a negative association between the length of basic education and the adjusted OR for having asthma.

The detailed effects of potential confounding variables on the occurrence of symptoms of oral diseases are presented in Tables 2.2–10.2 in Appendix 2. The strongest single factor affecting the most symptoms of oral disease was the concomitant use of medication other than for asthma. The effects of other possible confounders were modest or nil. The occurence of the symptom of dry mouth was higher among subjects older than 35 years than in younger subjects and also higher among smokers than non-smokers (Table 2.2). Smoking and age over 35 years were associated with the symptom of sore mouth (Table 3.2). Ex-smokers had higher OR for symptom of sore mouth compared to non-smokers while the difference between current smokers and non-smokers was smaller. Few of the potential confounding factors had a significant effect on halitosis (Table 4.2).

Women reported all TMJ symptoms slightly more often than men did (Tables 5–7.2), while other variables had negligible effects on the TMJ symptoms. Interestingly, frequent use of alcohol was also associated with low OR in pain in TMJ compared to subjects who had never used alcohol. From the three TMJ symptoms clicking was most often reported (Table 7.2).

From the potential confounding factors education and current smoking had a significant effect on toothache (Table 8.2). Males reported less sensitivity to hot, cold or sweet than females (Table 9.2). Again, education was associated with a higher probability of having this symptom. Smokers had lower prevalence of bleeding from gums than the subjects who had stopped smoking or the subjects who had newer smoked (Table 10.2). Interestingly, frequent use of alcohol was associated with increased probability of gingival bleeding compared to abstainers.

Taken together, generally the factors that were considered to be potential confounders had mainly slight effects on the probability of having symptoms of oral diseases. The only exception was the use of medication other than for asthma, which seemed to contribute significantly to four of the nine symptoms evaluated.

5.2.6 Evaluation of combined effects of asthma, allergy and asthma medication

The study population was further grouped according to the presence of asthma, allergy and asthma medication as described in Table 3. The numbers and percentages of subjects reporting oral symptoms are presented in Table 14. In the group of subjects having asthma, allergy and asthma medication simultaneously there were more subjects reporting symptoms of oral diseases than in any other group. The lowest occurrence for different symptoms for oral diseases was found among healthy subjects, with the exception of dry mouth, sore mouth and pain in TMJ. The lowest occurrence of these three symptoms was among subjects having asthma but not having asthma medication or allergy.

The crude ORs for having symptoms of oral diseases are shown in Table 15. In four symptoms (sore mouth, halitosis, pain in TMJ and stiffness in TMJ) out of nine, when compared to controls, highest crude ORs were obtained for subjects having asthma, allergy and asthma medication simultaneously.

The adjustment resulted in slightly lower ORs and wider confidence intervals, but the overall picture remained similar. The adjusted ORs for different oral symptoms are presented in Table 16. Presence of allergy was associated with slightly higher probability of having dry mouth compared to healthy, and subjects having both asthma and allergy had higher probability. Adding asthma medication led to even higher probability of dry mouth. However, the highest OR was found for asthmatic subjects having asthma and asthma medication but without allergy. Subjects with asthma, but without allergy and asthma medication had the lowest probability of dry mouth, even lower than the controls. Thus, it seems that allergy alone is not a very strong risk factor for dry mouth, but in combination with asthma it has some effect. The combination of asthma and asthma medication has the most profound effect on the probability of dry mouth. Comparing asthmatics with and without medication indicates that the use of asthma medication may be a risk factor for dry mouth.

For sore mouth the lowest probability was again found among asthmatics without asthma medication and allergy, but also subjects having allergy alone had low risk for sore mouth. The asthmatics having asthma medication had considerably higher probability but the adjusted OR was still fairly low. The combination of asthma and allergy had a strong effect and it was further strengthened if the subjects had all three risk factors simultaneously. Thus the combination of asthma, allergy and asthma medication seems to be the strongest risk factor for sore mouth. The finding that allergy alone is not a very strong risk factor is in contrast with Table 11 where allergic

Table 14. Number and proportion of subjects reporting symptoms of oral disease in Questionnaire Survey. The figures are presented for different categories of asthma (Group).

Group	All	Dry mouth	Sore mouth	Halitosis	Pain in TMJ	Stiffness in TMJ	Clicking in TMJ	Toothache	Sensitivity	Bleeding
Subjects without asthma, allergy and without asthma medication (Healthy).	486	55 11.3	30 6.2	108 22.2	9 1.9	12 2.5	41 8.4	38 7.8	137 28.2	157 32.3
Subjects with asthma, but without allergy and without asthma medication	61	4 6.6	3 4.9	19 31.1	1 1.6	4 6.6	7 11.5	7 11.5	20 32.8	18 29.5
Subjects without asthma and asthma medication but having allergy	107	16 15.0	6 5.6	29 27.1	7 6.5	5 4.7	26 24.3	10 9.3	41 38.3	45 42.1
Subjects without asthma and allergy but with asthma medication	5	4 80.0	1 20.0	0 0.0	0 0.0	1 20.0	0 0.0	0 0.0	1 20.0	2 40.0
Subjects with asthma and allergy, but without asthma medication	126	21 16.7	13 10.3	39 31.0	12 9.5	7 5.6	22 17.5	10 7.9	47 37.3	58 46.0
Subjects without asthma, but with allergy and asthma medication	3	0 0.0	0 0.0	1 33.3	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Subjects with asthma having asthma medication but without allergy	173	54 31.2	19 11.0	51 29.5	11 6.4	13 7.5	26 15.0	17 9.8	57 32.9	49 28.3
Subjects having asthma, allergy and asthma medication.	249	65 26.1	39 15.7	93 37.3	31 12.4	22 8.8	43 17.3	28 11.2	84 33.7	102 41.0

Table 15. Crude odds ratios and 95% confidence intervals for symptoms of oral diseases in different categories of asthma.

Group	Dry mouth	Sore mouth	Halitosis	Pain in TMJ	Stiffness in TMJ	Clicking in TMJ	Toothache	Sensitivity	Bleeding
Subjects without asthma, allergy and without asthma medication (Healthy).	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Subjects with asthma, but without allergy and without asthma medication	0.6 0.2 – 1.6	0.8 0.2 – 2.7	1.6 0.9 – 2.8	0.9 0.1 – 7.1	2.8 0.9 – 8.9	1.4 0.6 – 3.3	1.5 0.6 – 3.6	1.2 0.7 – 2.2	0.9 0.5 – 1.6
Subjects without asthma and asthma medication but having allergy	1.4 0.8 – 2.5	0.9 0.4 – 2.2	1.3 0.8 – 2.1	3.7 1.4 – 10.2	1.9 0.7 – 5.6	3.5 2.0 – 6.0	1.2 0.6 – 2.5	1.6 1.0 – 2.4	1.5 1.0 – 2.3
Subjects with asthma and allergy, but without asthma medication	1.6 0.9 – 2.7	1.8 0.9 – 3.5	1.6 1.0 – 2.4	5.6 2.3 – 13.6	2.3 0.9 – 6.0	2.3 1.3 – 4.0	1.0 0.5 – 2.1	1.5 1.0 – 2.3	1.8 1.2 – 2.7
Subjects with asthma having asthma medication but without allergy	3.6 2.3 – 5.4	1.9 1.0 – 3.4	1.5 1.0 – 2.2	3.6 1.5 – 8.8	3.2 1.4 – 7.2	1.9 1.1 – 3.2	1.3 0.7 – 2.3	1.2 0.9 – 1.8	0.8 0.6 – 1.2
Subjects having asthma, allergy and asthma medication.	2.8 1.9–4.1	2.8 1.7 – 4.7	2.1 1.5 – 2.9	7.5 3.5 – 16.1	3.8 1.9 – 7.9	2.3 1.4 – 3.6	1.5 0.9 – 2.5	1.3 0.9 – 1.8	1.4 1.1 – 2.0

Table 16. Adjusted odds ratios and 95% confidence intervals for symptoms of oral diseases in different categories of asthma, when all independent variables (age, gender, smoking, frequency of alcohol intake, place of residence, basic education, professional education, use of medication other than for asthma, and asthma) are retained in the model at the same time.

Group	Dry mouth	Sore mouth	Halitosis	Pain in TMJ	Stiffness in TMJ	Clicking in TMJ	Toothache	Sensitivity	Bleeding
Subjects without asthma, allergy and without asthma medication (Healthy).	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Subjects with asthma, but without allergy and without asthma medication	0.4 0.1 – 1.2	0.7 0.2 – 2.4	1.5 0.8 – 2.8	0.8 0.0 – 6.7	3.0 0.9 – 10.0	1.4 0.6 – 3.4	1.4 0.58 – 3.32	1.3 0.7 – 2.3	0.9 0.5 – 1.6
Subjects without asthma and asthma medication but having allergy	1.2 0.6 – 2.3	0.8 0.3 – 2.1	1.2 0.8 – 2.0	3.0 1.1 – 8.5	1.8 0.6 – 5.4	3.2 1.8 – 5.7	1.1 0.5 – 2.4	1.4 0.9 – 2.2	1.5 1.0 – 2.3
Subjects with asthma and allergy, but without asthma medication	1.5 0.9 – 2.6	1.7 0.9 – 3.5	1.6 1.0 – 2.4	5.2 2.1 – 12.8	2.3 0.9 – 6.2	2.3 1.3 – 4.1	0.9 0.4 – 2.0	1.4 0.9 – 2.1	1.7 1.1 – 2.6
Subjects with asthma having asthma medication but without allergy	2.1 1.3 – 3.4	1.2 0.6 – 2.3	1.4 0.9 – 2.1	2.4 0.9 – 6.2	2.7 1.3 – 6.6	1.7 0.9 – 2.9	1.2 0.6 – 2.2	1.1 0.8 – 1.7	0.8 0.6 – 1.3
Subjects having asthma, allergy and asthma medication.	1.9 1.2 – 2.9	2.2 1.3 – 3.9	2.0 1.4 – 2.9	4.5 2.0 – 10.1	2.7 1.2 – 6.0	1.9 1.2 – 3.2	1.4 0.8 – 2.4	1.1 0.8 – 1.6	1.4 1.0 – 2.0

subjects had significantly higher probability of reporting sore mouth. This is most probably due to residual confounding effect caused by the asthmatic subjects, who had allergy, and were included in this group. The lowest adjusted OR for having halitosis was found in subjects having allergy alone and, again, the highest probability for reporting halitosis was in subjects having all risk factors simultaneously.

Subjects having asthma alone had the lowest OR for having pain in the TMJ. Asthma together with asthma medication increased the risk of reporting pain in the TMJ considerably. Allergy alone seems to be a strong risk factor for this symptom. The effect of the combination of all three risk factors resulted in even higher adjusted OR, but the effect was not as strong as could be expected when comparing groups having allergy alone with groups having asthma with asthma medication. The highest effect was seen in the group having allergy and asthma but no asthma medication. In summary, allergy alone is a strong risk factor for having pain in the TMJ and asthma, with or without medication, increases risk further. Again, this is in contrast to Table 10, which shows fairly high adjusted OR for asthma. In this case this is probably because of the residual confounding due to allergy.

For stiffness in the TMJ the highest probability was in asthmatics who did not have allergy and asthma medication, but the 95% CI was fairly wide. Asthmatics having asthma medication had also high prevalence of this symptom, regardless whether they had allergy or not. Asthmatic subjects, with or without asthma medication, seem to have increased risk of stiffness in the TMJ, while allergy played minor role. Allergy was the most significant risk factor for reporting of clicking in the TMJ but slightly increased risk was found in all subgroups. Interestingly, the co-morbidity with asthma and allergy led to decreased probability compared to allergy alone

Prevalence of toothache, as well as sensitivity to hot, cold or sweet, was quite equally distributed across the groups and none of the groups had significantly higher probability for these symptoms. Gingival bleeding was strongly connected to the presence of allergy and the combination of asthma and allergy had even higher probability of having gingival bleeding. Interestingly, in subjects having all three risk factors simultaneously this symptom was less common than among subjects having allergy and asthma but no asthma medication.

6 Discussion

The results from the Pilot Study support the hypothesis that asthma may increase the risk for inflammatory periodontal diseases. Asthmatics in the Pilot Study also had significantly lower stimulated salivary flow rate compared to healthy subjects The findings from the Questionnaire Survey indicate that adult asthmatics also suffer more often from the symptoms of certain oral diseases than non-asthmatic adult controls. In six symptoms (dry mouth, sore mouth, halitosis, pain in TMJ, stiffness in TMJ, and clicking in TMJ) out of nine, asthmatics had significantly higher probability of having the symptom compared to the healthy subjects.

The Pilot Study was the first published report on the oral health, salivary flow rate and saliva composition of adult asthmatic patients. However, this study shares the same problem as many of the earlier studies in children and adolescents: the measurements are based on a fairly small number of subjects. Another drawback in the Pilot Study was that the dental check-ups were not performed in a blind manner, which may bias the results.

The major advantage of the Questionnaire Survey was the relatively large number of observations, which increases the credibility of the results. On the other hand, the response rate in the Questionnaire Survey was 61.7%, which is clearly lower than e.g. that of the KELA Survey, 72.7% (Aalto et al. 1999). This raises the question of how representative the study population is. The comparison of the demographic data of these two surveys reveals that at least the gender distributions are close to each other. However, the asthmatics in the Questionnaire Survey were somewhat younger and there were also differences in the distributions of basic education and professional education. In the Questionnaire Survey the percentage of subjects having longer education and a higher level of professional education was greater than in the KELA Survey.

The validity of the questionnaire always remains crucial when estimating the scientific value of the results from questionnaire studies. One option to estimate the validity of the questionnaire used in the Questionnaire Survey is by comparing the results of this study against those published earlier by other researchers. The similarity of the results between the Questionnaire Survey and other studies concerning e.g. gender distribution, smoking habits, or prevalence of certain symptoms in the control

group indicates that the results reported here are in line with the results from other studies. However, it has to be kept in mind that this is only indirect evidence for the validity of the questionnaire. Many of the findings reported here are unique and cannot be compared to previous research. Other researchers inspired by this study will hopefully confirm these results. The questions used in the evaluation of symptoms of oral diseases were obtained from the standard questionnaire used by dentists in their daily practice in order to collect oral health data for the planning of treatment.

In the Questionnaire Survey altogether 187 of the 610 asthmatics did not use any type of asthma medication. According to personal communication, KELA estimates that approximately 20% of the subjects in the register do not take medications regularly. Because the register is cumulative in nature, subjects who are once included to the register, will not be removed if they temporarily stop taking medication. The percentage of asthmatics without medication in the Questionnaire Survey was 31%. The higher percentage can be explained by the age of the subjects; in the Questionnaire Survey the age of the subjects ranged from 20 to 55 years and usually the disease is more severe in children or in old people, groups that were excluded from this study. The fluctuation of disease severity over time, as well as the fluctuation in the need for anti-asthma medication, are characteristic of asthma. However, this group of asthmatics does have diagnosed asthma even though they reported not using anti-asthma medication at the time of survey. Thus this group was suitable for the evaluation of the "asthma without medication" effect on the symptoms of oral diseases.

In the Pilot Study the asthmatic subjects had significantly more periodontal disease than healthy subjects. This is in accordance with earlier studies, where a similar association has been described between asthmatic and non-asthmatic children (Hyyppä et al. 1979, McDerra et al. 1998). In the Questionnaire Survey slightly more gingival bleeding was reported by asthmatics than by non-asthmatics. However, the detailed analysis showed that the reason for higher probability for having gingival bleeding was due to co-existing allergy rather than asthma itself. Spontaneous gingival bleeding is regarded as a cardinal sign of gingivitis, although it may not always predict advanced periodontal disease quite well. There exists only one report about the prevalence of periodontal diseases in atopics. The published report indicates that atopic subjects may have an increased risk for gingivitis (Mattson and Möller 1990). The findings from the Questionnaire Survey support the findings of Mattson and Möller.

In periodontal diseases the host response via the immune defence system is considered important (Seymour et al. 1996). Cellular immunity has been implicated in periodontal destruction for over 25 years (Niesengard 1977, Genco and Slots 1984, Hernichel-Gorbach 1994, Gammel et al. 1997). Although the role of allergy is not clear, IgE mediated mechanisms are assumed to be involved in the pathogenesis of gingival and periodontal diseases (Niesengard 1977, Hyyppä 1984). In patients having birch pollen allergy, an increased amount of gingivitis was observed during the pollen season when compared with the off-season (Mattson and Möller 1990). Platelet-activating factor, one of the mediators of allergic inflammatory reaction (Chung 1997, Page 1988), is also present in inflamed gingival tissues (Noguchi et al. 1989). Interestingly, some of the cytokines which mediate inflammatory processes in the mucous membranes of airways (Chung and Barnes 1999) are also found in inflamed periodontal tissues. Gingival and peripheral mononuclear cells obtained from adult patients with chronic periodontitis can produce increased amounts of interleukin (IL) –5 and IL-6 (Fujihashi et al. 1993, Sigusch et al. 1998). The possible co-existence of allergy and periodontal diseases may thus be explained by the fact that they have common features in their pathophysiology.

The Pilot Study showed that paraffin-stimulated flow rate of whole saliva is decreased in adult asthmatic patients compared to non-asthmatic controls. The 24% reduction in flow rate of stimulated whole saliva in adult asthmatic patients is of about the same magnitude as that reported for asthmatic children and adolescents (Bjerkeborn et al. 1987, Ryberg et al. 1987, 1991). An even larger reduction has been reported for stimulated parotid saliva (Ryberg et al. 1987, 1991). In the Questionnaire Survey the asthmatic subjects had significantly higher probability of having dry mouth than healthy subjects. When the combined effects of all three risk factors (asthma, allergy and asthma medication) were analysed in the same model, it was found that subjects having asthma alone had the lowest probability for dry mouth, but the use of asthma medication was associated with significantly higher risk. This is in accordance with the finding of Bergdahl and Bergdahl (2000). In their study low unstimulated salivary flow rate and subjective oral dryness were significantly associated with the use of anti-asthmatic drugs.

The decrease in salivary flow rate among asthmatics has previously been linked to the regular use of inhaled β_2-agonists (Rydberg et al. 1990, 1991). The regulation of salivary synthesis and secretion is a rather complex system, involving at least

adrenergic, cholinergic and non-adren-non-cholinergic nerves (Ekström 1989). Adrenergic nerves primarily regulate protein synthesis in salivary glands (Suddick and Dowd 1980), and the stimulation of β-receptors of salivary gland cells in vivo leads to enhanced protein synthesis (Baum et al. 1984). Asthmatics in the present study used inhaled β_2-agonists on an as needed –basis and were less exposed to those medications than the asthmatics in earlier studies. Thus the use of β_2-agonists may not be the only explanation for the decreased stimulated salivary flow rate. The are no reports available about the effects of ICS on the function of the salivary glands but in the lungs one of the effects of ICS is decreased mucous secretion (Barnes and Pedersen 1993).

There are no published reports available concerning the prevalence of dry mouth in asthmatic population. In the Questionnaire Survey the prevalence of dry mouth in asthmatic population was 24%, which corresponds well with the prevalence reported in medicated adult population in age groups from 20 to 50 years, in a large population-based survey in Sweden (Nederfors 1996). In that study the prevalence of symptoms of dry mouth in the non-medicated population ranged from 10.1 to 19.6%, which is about the same as the prevalence of dry mouth in healthy subjects in Questionnaire Survey – a prevalence of 12%.

The concomitant use of medication other than for asthma was a strong confounding factor for dry mouth. This is in agreement with the findings from Nederfors (1996), that the polypharmacy is a true risk factor for oral dryness. The use of medication other than for asthma was also a significant risk factor for the prevalence of other symptoms of oral diseases. On the other hand, the use of medication other than for asthma was more common among asthmatics than controls. The medications used are not known exactly, but the most likely explanation is the co-morbidity of allergic diseases. Asthmatics often tend to use medications for other allergic conditions, such as rhinitis, conjunctivitis, and dermatitis. However, the possible co-morbidity of other than atopic diseases cannot be excluded, and is an interesting option for further research.

In the Pilot Study no difference in DMFT values between the asthmatics and controls was found. There are several publications where a positive association between asthma and caries has been reported, but recently, however, the association between caries and childhood asthma has been questioned (Shulman et al. 2001, Meldrum et al. 2001). In the Pilot Study there were more subjects among asthmatics having two or more decayed teeth than among healthy subjects, indicating differences in caries morbidity. This supports the findings of McDerra et al. (1998) regarding the significant

difference in the severity and number of teeth affected by tooth surface loss between asthmatic and non-asthmatic children.

An interesting finding was the relationship between asthma, allergy and symptoms of TMJ disorders. It is worth noting that different TMJ symptoms were associated in a different way with asthma and allergy. Pain in the TMJ and clicking in the TMJ were mainly associated with allergy, while stiffness in the TMJ was more common in asthmatic subjects. The possible mechanisms behind these associations are not clear. There is some indirect evidence about the link between mouth breathing and malocclusion. Mouth breathing caused by nasal obstruction is supposed to affect facial growth (Rubin 1980) leading to possible malocclusion. There is evidence that the spatial relationship of the mandible to the craniomaxillary complex is influenced, in part, by the function of the muscular elevators of the mandible. One factor that acts on the elevators of the mandible is the rest position of the mandible, which may be influenced by the patient's mode of respiration like mouth breathing (Rubin 1980). Hannuksela and Väänänen (1987) showed in their study that atopy is associated with posterior cross-bites, and in another survey from India posterior crossbite correlated with mouth breathing (Corruccini et al. 1985). In a study by Kairaitis et al. (1999) it was shown that asthmatics have a greater tendency to mouth breathing than non-asthmatic subjects. The aetiology of TMJ dysfunction still remains a matter of controversy. On the other hand there is no clear evidence for the association between malocclusion and TMJ dysfunction (McNeill 2000) but the theories proposed include the spatial relationship between mandible and maxilla as a major reason for the aetiology for TMJ disorders (Mew 1997). Recently there has been growing interest in the research of tissue reactions in TMJ dysfunction. It seems that pain in the TMJ is caused by inflammatory changes in joint tissues leading to arthritis and tissue destruction. In this process cytokines are of utmost importance (Alstergren 2000) and at least IL-6 has been proposed as one major cytokine found in the synovial fluid of patients with chronic TMJ disorders (Shinoda and Takaku 2000).

In the Questionnaire Survey males had lower probability of having asthma compared to females. An epidemiological report from Finland shows that asthma is slightly more common among adult females than among adult males (Huovinen et al. 1999), but the difference was somewhat smaller than in our study. Recently another questionnaire survey (the KELA Survey) evaluating the health status, use of health services and need for rehabilitation among people with asthma was published in Finland

(Aalto et al. 1999). This study was performed shortly after the Questionnaire Survey. In the KELA Survey the proportion of males was 36.5% compared to 38.7% in the Questionnaire Survey. In both surveys females seemed to be over-represented in the asthma population, probably due to different behaviour in responding to this type of questionnaire.

Although smoking is a known risk factor for several oral diseases, the effects of smoking on the symptoms of oral diseases have not been extensively reported. Among the asthmatics the proportion of current smokers was 27%, which is about on the same level as reported in the KELA Survey – 30% including regular and occasional smokers. In the Questionnaire Survey the probability of oral dryness was increased in current smokers. This contradicts another report indicating that smoking does not affect salivary flow rate (Parvinen 1984). However, the relationship between subjective feeling of dry mouth (xerostomia) and objective finding of decreased salivary flow rate (hyposalivation) does not necessarily correlate (Fox et al. 1987). Subjects having normal salivary flow rate may feel symptoms of dry mouth because of mouth breathing that occurs e.g. when having a blocked nose. The feeling of xerostomia may also be more related to the condition of oral mucous membranes than to pathologically decreased salivary flow rate.

Those who had stopped smoking reported more symptoms of sore mouth and the probability of this symptom was even higher than among smokers. Current smokers also had increased probability of reporting toothache. Although smokers tend to have more caries (Axelsson et al. 1998, Hahn et al. 1999, Unell et al. 1999, Sgan-Cohen et al. 2000), the direct effect of smoking on caries development has not been reported. The association found may reflect different health behaviour rather than the effects of smoking on the development of caries. In an epidemiological study in Finland, Sakki et al. (1998) studied the association of lifestyle (physical activity, tobacco smoking, alcohol consumption and dietary habits) with dental caries, periodontal health, denture stomatitis and dental health behaviour. In this study an unhealthy lifestyle was associated with higher amount of dental decay, periodontal disorders, and a higher prevalence of denture stomatitis. The study evaluating interactions between people's diet and their smoking habits showed that smokers had a tendency to use more sugar than non-smokers in their daily diet (Margetts and Jackson 1993).

Current smokers reported less gingival bleeding compared to ex-smokers or non-smokers. Smoking is a known risk factor for advanced periodontal diseases (Johnson

and Slach 2001, Bergström et al. 2000) but gingival bleeding is less common among smokers than non-smokers (Bergström and Boström 2001), probably due to the suppressive effect of smoking on peripheral circulation. In the Questionnaire Survey the frequent use of alcohol increased the probability of gingival bleeding. Poor oral hygiene is a common risk factor for gingival bleeding and this finding may be explained by the general lifestyle (Sakki et al. 1998).

Previously it has been shown that allergy itself may cause burning and painful sensations on mucous membranes in the oral cavity in connection to exposure to allergens, especially in food allergies (Pastorello et al. 1995). In the Questionnaire Survey allergy alone was not a significant risk factor for sore mouth, but the combination of asthma, asthma medication and allergy led to highest probability for reporting sore mouth. One of the reported side-effects of inhaled corticosteroids is sore throat. The direct effects of inhaled steroids on oral mucous membranes are not known. However, the use of inhaled corticosteroids may sometimes increase the risk of candida infections in mouth (Toogood 1990), a condition that is also occasionally associated with painful feeling in oral mucous membranes. Often the reason for sore mouth remains unclear, but it is worth noting that in several reports and reviews, dry mouth has been proposed as one possible factor contributing to this syndrome.

Halitosis was a common problem, 22% of controls reported having halitosis. There are no reports available on the prevalence of halitosis in asthmatic population. In this study the prevalence of halitosis was highest among asthmatics who had all the three risk factors simultaneously.

7 Conclusions

The main findings from the Pilot Study and Questionnaire Survey can be enumerated as follows:

1. The results of these studies support the hypothesis that asthmatic subjects have increased risk for oral diseases and that they also report more symptoms of oral diseases than non-asthmatic subjects. Based on the findings from the Pilot Study adult asthmatic subjects suffer more from periodontal disease and they have lower stimulated salivary flow rate than non-asthmatic adult subjects. Based on the findings from the Questionnaire Survey adult asthmatic subjects report more subjective symptoms of oral dryness, sore mouth, halitosis, and TMJ disorders than non-asthmatic subjects.
2. When comparing asthmatics and controls in terms of oral health, factors related to asthma (atopy, asthma medication) have to be taken into account. The underlying cause in TMJ disorders and gingival bleeding seems to be co-existing allergy. On the other hand, the reported symptoms of oral dryness could be attributed to the medication used in the treatment of asthma. The latter may also indicate the effect of disease severity rather than the effect of medication itself. In general, subjects having all three risk factors (asthma, allergy and asthma medication) simultaneously, tended to have the highest probabilities for symptoms of oral diseases.
3. The factors studied in the Questionnaire Survey as potential confounding factors had mainly slight effects on the probability of having symptoms of oral diseases. The marked exception was the concomitant use of medication other than for asthma, which markedly increases the probability of symptoms of several different oral diseases. This must be taken into account as an important confounding factor when studies on oral health are planned, especially in the adult population.

The clinical implications of the findings are that adult asthmatic patients having allergy and regular anti-asthmatic treatment with inhaled medications also need special attention in oral health care. Co-operation between pulmonologists, asthma nurses and oral health care team is also warranted.

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Appendix 1

KYSELYLOMAKE SUUN TERVEYDENTILAN TUTKIMUSTA VARTEN

Ennenkuin vastaatte tässä kyselylomakkeessa esitettyihin kysymyksiin lukekaa täyttöohjeet huolellisesti!

26.2.1996

Kari Laurikainen
Terveystieteen laitos
Tampereen Yliopisto

TÄYTTÖOHJEET

1) Lukekaa huolellisesti läpi koko kysymys ja kaikki annetut vastausvaihtoehdot. Useimmissa kysymyksissä on annettu useita vastausvaihtoehtoja valmiiksi. Kunkin vaihtoehdon edessä on numero. Ympyröikää sen vaihtoehdon numero, joka Teidän mielestänne on oikea.
2) Mikäli merkitsitte väärän vaihtoehdon ja haluatte korjata, vetäkää viiva väärän numeron päälle ja ympyröikää sen jälkeen oikea vaihtoehto.
3) Mikäli pyydetään kirjoitettua vastausta, kirjoittakaa selvästi, mieluiten tekstaten. Käyttäkää sinistä tai mustaa kuulakärkikynää.
4) Palauttakaa täytetty kyselylomake oheista palautuskuorta käyttäen. Ennen palautusta tarkistakaa, että olette vastannut kaikkiin kohtiin.
5) Osa kyselyyn vastanneista kutsutaan ilmaiseen hammaslääkärin tarkastukseen. Siksi on tärkeätä, että täytätte myös alla olevan Suostumus-kohdan ennen kuin palautatte lomakkeen. Osallistuminen tarkastukseen on täysin vapaaehtoista. Mikäli ette halua, että Teidät kutsutaan ao tarkastukseen, voitte siitä huolimatta täyttää ja palauttaa kyselylomakkeen. Joihinkin, jotka ovat suostuneet mahdolliseen tarkastukseen, otetaan myöhemmin yhteyttä.

Tutkimuksessa saatuja tietoja käsitellään luottamuksellisesti ja käytetään vain tieteellisiin tarkoituksiin! Tutkimuksesta saatuja tietoja voidaan myäs yhdistellä muista terveydenhuollon rekistereistä saatuihin tietoihin.

SUOSTUMUS

Rastittakaa allaolevista oikea vaihtoehto.

____ Suostun / ____ En suostu, että minut voidaan kutsua ilmaiseen hammaslääkärin tarkastukseen myöhemmin ilmoitettavana ajankohtana.

Mikäli suostutte, ilmoittakaa yhteystietonne allaoleville riveille!
Nimi: _____
Osoite: _____
Puhelin: _____ (Koti) _____ (Työ)
Päiväys: _____ Allekirjoitus: _____

KYSELYLOMAKE **Havaintotunnus (tutkija täyttää) _____**

Tälle lomakkeelle antamanne tiedot käsitellään luottamuksellisesti!

1. Sukupuoli

0 Nainen
1 Mies

2. Syntymävuosi: 19____

3. Koulutus
1 Kansakoulu
2 Keskikoulu tai peruskoulun ylä-aste
3 ylioppilastutkinto

4. Ammatillinen koulutus
1 Ei ammattikoulutusta
2 Ammattikurssi tai työpaikalla saatu koulutus
3 Ammattikoulu
4 Koulutasoinen tutkinto (esimerkiksi teknikko)
5 Opistotasoinen tutkinto (esimerkiksi merkonomi)
6 Korkeakoulu- tai yliopistotutkinto
7 Opiskelija

5. Nykyinen ammattinne?
Mikäli olette tällä hetkellä työtön tai eläkkeellä, ilmoittakaa se ammatti, jossa viimeksi olette toiminut.

_____

6. Nykyinen asuinympäristönne?
1 Maaseutu (haja-asutusalue tai kylä)
2 Taajama (kirkonkylä tai kaupunkimainen ympäristö)

7. Tupakointi
0 En ole koskaan tupakoinut
1 Olen lopettanut tupakoinnin
2 Tupakoin

Mikäli ette ole koskaan tupakoinut, voitte siirtyä kysymykseen 11!

8. Milloin aloititte tupakoinnin?

Vuonna _____

9. Jos olette lopettanut niin milloin?

Vuonna _____

10. Tupakoinnin määrä nyt tai silloin kun lopetitte tupakoinnin
Arvioikaa tupakoinnin määrä päivässä, viikossa tai kuukaudessa ja merkitkää se siihen ajanjaksoon, mikä tuntuu sopivimmalta. Mikäli poltatte useampaa lajia, ympyröikää oikeat vaihtoehdot (ja / tai)

___ savuketta/vrk ___ savuketta/vko ___ savuketta/kk ja / tai

___ sikaaria/vrk ___ sikaaria/vko ___sikaaria/kk ja / tai

___ piipullista/vrk ___ piipullista/vko ___ piipullista/kk

11. Kuinka usein juotte alkoholia sisältäviä juomia?
0 En käytä lainkaan alkoholia
1 Satunnaisesti, kerran kuukaudessa tai harvemmin
2 2-4 kertaa kuukaudessa
3 2-3 kertaa viikossa
4 neljä kertaa viikossa tai useammin

Mikäli ette käytä lainkaan alkoholia, voitte siirtyä suoraan kysymykseen 14!

12. Kuinka monta alkoholia sisältävää juoma-annosta käytätte tavallisesti silloin, kun nautitte alkoholia? Mikäli ilmoitatte useampaa lajia ympyröikää oikeat vaihtoehdot (ja / tai).

___ pulloa keskiolutta ja / tai

___ pulloa A-olutta ja / tai

___ lasillista viiniä (Yksi pullo on noin 6 lasillista) ja / tai

___ annosta väkevää alkoholia (1/2 litran pullo on 12 annosta)

13. Kuinka kauan on siitä, kun olette viimeksi nauttinut alkoholia?
1 Yli puoli vuotta
2 1-6 kuukautta
3 1-4 viikkoa
4 1-6 päivää

14. Kuinka usein syötte makeisia? (Myös kurkkupastillit lasketaan makeisiksi)
0 En lainkaan
1 Kerran viikossa tai harvemmin
2 2-6 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

15. Valitsetteko ksylitolilla makeutettuja makeisia?
0 Aina kun mahdollista
1 Toisinaan
2 En koskaan

16. Juotteko sokeroituja virvoitusjuomia tai mehuja?
0 En lainkaan
1 Kerran viikossa tai harvemmin
2 2-6 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

17. Käytättekö sokeria kahvin kanssa?
0 En juo kahvia / En käytä sokeria kahvin kanssa
1 Kerran viikossa tai harvemmin
2 2-4 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

18. Käytättekö sokeria teen kanssa?
0 En juo teetä / En käytä sokeria teen kanssa
1 Kerran viikossa tai harvemmin
2 2-4 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

19. Käytättekö sokeria kaakaon kanssa? (Huom! Valmiit maitokaakaoseokset sisältävät myös sokeria)
0 En juo kaakaota / En käytä sokeria kaakaon kanssa
1 Kerran viikossa tai harvemmin
2 2-4 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

20. Syöttekö makeita leivonnaisia?
0 En lainkaan
1 Kerran viikossa tai harvemmin
2 2-6 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

21. Syöttekö tuoreita vihanneksia ja/tai raasteita?
0 En lainkaan
1 Kerran viikossa tai harvemmin
2 2-6 kertaa viikossa
3 Päivittäin kerran tai kahdesti
4 Päivittäin useammin kuin kahdesti

22. Noudatatteko jotain erityisruokavaliota? Ympyröikää kaikki oikeat vaihtoehdot.
0 En noudata erityisruokavaliota
1 Kasvisruokavalio
2 Elävä ravinto
3 Gluteiiniton ruokavalio
4 Laktoositon ruokavalio
5 Muu erikoisruokavalio, mikä? _____

23. Kuinka usein harjaatte hampaanne?
0 En harjaa hampaitani lainkaan
1 Toisinaan
2 Joka toinen päivä
3 Kerran päivässä
4 Kaksi kertaa päivässä tai useammin

24. Käytättekö fluoripitoista hammastahnaa?
0 En käytä
1 Kyllä käytän
2 En tiedä

25. Käytättekö fluoripitoisia suuvesiä?
0 En käytä
1 Käytän toisinaan
2 Käytän viikottain
3 Käytän päivittäin
4 En tiedä

26. Käytättekö hammastikkuja hampaiden puhdistamiseen?
0 En käytä
1 Käytän toisinaan
2 Käytän viikottain
3 Käytän päivittäin

27. Käytättekö hammaslankaa hampaiden puhdistamiseen?
0 En käytä
1 Käytän toisinaan
2 Käytän viikottain
3 Käytän päivittäin

28. Kuinka usein käytte hammaslääkärillä?
0 Vain kun on kipua tai vaivaa
1 Harvemmin kuin joka toinen vuosi.
2 Harvemmin kuin kerran vuodessa mutta vähintaan joka toinen vuosi.
3 Kerran vuodessa tai useammin

29. Onko hammaslääkäri käsitellyt hampaitanne fluoripitoisilla hoitoaineilla hoidon yhteydessä?
0 Ei
1 Kyllä
2 En tiedä

30. Milloin olette viimeksi käynyt hammaslääkärin vastaanotolla?

Vuonna _____

31. Mitä mieltä olette nykyisestä terveydentilastanne?
1 Erittäin hyvä
2 Hyvä
3 Tyydyttävä
4 Huono
5 Erittäin huono

32. Onko Teillä todettu jokin seuraavista sairauksista tai oireista. Kysymykseen tulevat lääkärin toteamat sairaudet tai oireet. Ympyröikää kaikki sairautenne ja oireenne sekä ilmoittakaa vuosi, milloin todettu. Mikäli ei mitään ole todettu, ympyröikää kohta 15.

Sairaus tai oire	Todettu vuonna?
1 Sydän- tai verisuonisairaus	_____
2 Kohonnut verenpaine	_____
3 Sokeritauti	_____
4 Astma	_____
5 Muu keuhkosairaus	_____
6 Allergia	_____
7 Kilpirauhasen sairaus	_____
8 Reuma	_____
9 Mahahaava	_____
10 Munuaissairaus	_____
11 Maksasairaus	_____
12 AIDS/HIV	_____
13 Epilepsia	_____
14 Psyykkinen sairaus	_____
15 Ei ole todettu mitään edellisistä	

33. Käytättekö irroitettavaa hammasproteesia? Ilmoittakaa myös proteesin laatu (osa- tai kokoproteesi)

0 En käytä irroitettavaa hammasproteesia
1 Käytän yläleuassa: ___ Osaproteesi ___ Kokoproteesi
2 Käytän alaleuassa: ___ Osaproteesi ___ Kokoproteesi

34. Pystyttekö pureskelemaan ruuan mielestänne riittävän tehokkaasti?
0 En pysty
1 Kyllä pystyn
2 En osaa sanoa

35. Onko Teillä ollut viimeisten kolmen kuukauden aikana jokin / jotkin seuraavista oireista? Ympyröikää kaikki Teillä esiintyneet oireet.

1 Päänsärkyä
2 Lihassärkyä
3 Särkyä nivelissä
4 Hengitysvaikeuksia
5 Hengityksen vinkunaa
6 Nenän tukkoisuutta
7 Aivastelua
8 Vesinuhaa
9 Poskiontelotulehdusta
10 Kurkkutulehdusta
11 Yskimistä
12 Limantuloa keuhkoista
13 Taiveihottumaa
14 Maitorupea
15 Nokkosihottumaa
16 Mahavaivaa
17 Närästystä tai ylävatsavaivoja
18 Suun kuivumista
19 Suun ja kielen kirvelyä
20 Pahaa makua tai hajua suussa
21 Kipua leukanivelissä
22 Jäykkyyttä leukanivelissä
23 Naksumista tai rahinaa leukanivelissä
24 Hammassärkyä
25 Hampaiden vihlomista kylmälle, kuumalle tai makealle
26 Verenvuotoa ikenistä esimerkiksi hampaita harjatessa

36. Käytättekö jatkuvasti lääkärin reseptillä määräämiä lääkkeitä?
0 Ei
1 Kyllä

37. Mikäli vastasitte edelliseen kysymykseen "Kyllä", kirjoittakaa allaoleville viivoille käyttämänne lääkkeet (Nimi, vahvuus, montako tablettia/annosta/suihketta päivittäin käytätte). Kirjoittakaa lääkkeiden nimet mahdollisimman selvästi!

Lääke	Vahvuus	Annoksia/päivä
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

KIITOKSIA VAIVANNÄÖSTÄNNE!

Ennen kuin palautatte tämän kyselylomakkeen, tarkistakaa, että olette vastanneet kaikkiin kohtiin ja että olette täyttänyt myös lomakkeen alussa olevan Suostumus-kohdan.

Appendix 2

Tabulated results of the analysis of potential confounding effects of selected background variables

Table 1.2. Number of asthmatics in different categories of potential confounding variables in Questionnaire Survey. Crude and adjusted ORs and 95% confidence interval for adjusted ORs for independent variables (age, gender, smoking, frequency of alcohol intake, place of residence, basic education, professional education, and concomitant use of medication other than for asthma) are presented. In the calculation of adjusted ORs all independent variables are simultaneously retained in the model.

Confounder	Number of subjects		ORcrude	ORadj	95%CI
	Asthmatics	Healthy			
Age (years)					
< 35	294	343	1.0	1.0	
35 or more	317	263	1.4	1.1	0.8 – 1.5
Gender					
Female	376	341	1.0	1.0	
Male	235	265	0.8	0.8	0.6 – 1.1
Smoking					
Never	271	298	1.0	1.0	
Stopped	175	137	1.4	1.4	1.0 – 1.8
Smoker	163	170	1.0	1.1	0.8 – 1.5
Alcohol					
Never	64	53	1.0	1.0	
Moderate	458	456	0.8	1.0	0.6 – 1.5
High	88	96	0.8	0.8	0.5 – 1.4
Residence					
Rural	87	64	1.0	1.0	
Urban	522	541	0.7	0.8	0.5 – 1.1
Basic education					
< 9 years	203	142	1.0	1.0	
9 years	220	212	0.7	0.9	0.6 – 1.3
12 years	188	251	0.5	0.6	0.4 – 0.9
Professional education					
Lower	189	148	1.0	1.0	
Intermediate	187	185	0.8	1.0	0.7 – 1.3
Upper	174	208	0.7	1.1	0.7 – 1.5
Students	53	54	0.8	1.3	0.8 – 2.2
Use of medication other than for asthma					
No	373	516	1.0	1.0	
Yes	236	85	3.8	3.4	2.6 – 4.6

Table 2.2. Numbers of subjects with or without symptoms of dry mouth in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	550	87	1.0	1.0	
35 or more	447	133	1.9	1.3	0.9 – 1.9
Gender					
Female	585	132	1.0	1.0	
Male	412	88	1.0	1.0	0.7 – 1.4
Smoking					
Never	484	85	1.0	1.0	
Stopped	247	65	1.5	1.3	0.9 – 1.9
Smoker	264	69	1.5	1.5	1.0 – 2.3
Alcohol					
Never	91	26	1.0	1.0	
Moderate	750	164	0.8	1.0	0.6 – 1.6
High	154	30	0.7	0.9	0.4 – 1.7
Residence					
Rural	121	30	1.0	1.0	
Urban	874	189	0.9	1.0	0.6 – 1.5
Basic education					
< 9 years	259	86	1.0	1.0	
9 years	349	83	0.7	1.0	0.7 – 1.6
12 years	388	51	0.4	0.7	0.4 – 1.2
Professional education					
Lower	452	131	1.0	1.0	
Upper	528	87	0.6	0.8	0.6 – 1.2
Concomitant use of medication other than for asthma					
No	776	113	1.0	1.0	
Yes	215	106	3.4	2.5	1.8 – 3.6

Table 3.2. Numbers of subjects with or without symptoms of sore mouth in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders are kept in the model at the same time.

	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	593	44	1.0	1.0	
35 or more	511	69	1.8	1.6	1.0 – 2.7
Gender					
Female	646	71	1.0	1.0	
Male	458	42	0.8	0.9	0.6 – 1.4
Smoking					
Never	529	40	1.0	1.0	
Stopped	271	41	2.0	1.8	1.1 – 3.0
Smoker	302	31	1.4	1.3	0.8 – 2.3
Alcohol					
Never	104	13	1.0	1.0	
Moderate	828	86	0.8	0.9	0.4 – 1.7
High	171	13	0.6	0.5	0.2 – 1.2
Residence					
Rural	130	21	1.0	1.0	
Urban	970	92	0.6	0.6	0.4 – 1.0
Basic education					
< 9 years	305	40	1.0	1.0	
9 years	390	42	0.8	1.2	0.7 – 2.2
12 years	408	31	0.6	1.2	0.6 – 2.3
Professional education					
Lower	518	65	1.0	1.0	
Upper	568	47	0.7	0.8	0.5 – 1.3
Concomitant use of medication other than for asthma					
No	825	64	1.0	1.0	
Yes	274	47	2.2	1.7	1.1 – 2.7

Table 4.2. Numbers of subjects with or without symptoms of halitosis in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	449	188	1.0	1.0	
35 or more	424	156	0.9	0.7	0.5 – 1.0
Gender					
Female	509	208	1.0	1.0	
Male	364	136	0.9	0.9	0.7 – 1.2
Smoking					
Never	423	146	1.0	1.0	
Stopped	212	100	1.4	1.3	0.9 – 1.8
Smoker	236	97	1.2	1.1	0.8 – 1.5
Alcohol					
Never	83	34	1.0	1.0	
Moderate	654	260	1.0	0.9	0.6 – 1.4
High	135	49	0.9	0.8	0.5 – 1.4
Residence					
Rural	104	47	1.0	1.0	
Urban	766	297	0.9	0.9	0.6 – 1.3
Basic education					
< 9 years	240	105	1.0	1.0	
9 years	302	130	1.0	0.9	0.6 – 1.3
12 years	330	109	0.8	0.8	0.5 – 1.3
Professional education					
Lower	399	184	1.0	1.0	
Upper	459	156	0.7	0.8	0.5 – 1.0
Concomitant use of medication other than for asthma					
No	653	236	1.0	1.0	
Yes	217	104	1.3	1.1	0.8 – 1.0

Table 5.2. Numbers of subjects with or without symptoms of pain in TMJ in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	601	36	1.0	1.0	
35 or more	545	35	1.1	0.9	0.5 – 1.7
Gender					
Female	663	54	1.0	1.0	
Male	483	17	0.4	0.6	0.3 – 1.0
Smoking					
Never	537	32	1.0	1.0	
Stopped	293	19	1.1	1.1	0.6 – 2.1
Smoker	314	20	1.1	1.4	0.7 – 2.6
Frequency of alcohol intake					
Never	105	12	1.0	1.0	
Moderate	860	54	0.6	0.6	0.3 – 1.2
High	179	5	0.2	0.3	0.0 – 0.9
Residence					
Rural	142	9	1.0	1.0	
Urban	1002	61	1.0	1.1	0.5 – 2.3
Education					
< 9 years	323	22	1.0	1.0	
9 years	402	30	1.1	1.3	0.7 – 2.7
12 years	420	19	0.7	0.8	0.3 – 1.9
Professional education					
Lower	549	34	1.0	1.0	
Upper	579	36	1.0	1.1	0.6 – 2.1
Concomitant use of medication other than for asthma					
No	855	34	1.0	1.0	
Yes	284	37	3.3	2.5	1.5 – 4.4

Table 6.2. Numbers of subjects with or without symptoms of stiffness in TMJ in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	606	31	1.0	1.0	
35 or more	547	33	1.2	0.8	0.4 – 1.6
Gender					
Female	669	48	1.0	1.0	
Male	484	16	0.4	0.5	0.3 – 1.0
Smoking					
Never	562	34	1.0	1.0	
Stopped	296	16	0.8	0.7	0.4 – 1.4
Smoker	319	14	0.7	0.7	0.4 – 1.4
Alcohol					
Never	109	8	1.0	1.0	
Moderate	865	49	0.8	1.0	0.4 – 2.3
High	177	7	0.5	0.8	0.3 – 2.6
Residence					
Rural	146	5	1.0	1.0	
Urban	1005	58	1.7	1.8	0.7 – 4.6
Education					
< 9 years	323	22	1.0	1.0	
9 years	408	24	0.9	0.9	0.4 – 1.9
12 years	421	18	0.6	0.6	0.2 – 1.4
Professional education					
Lower	533	30	1.0	1.0	
Upper	582	33	1.0	1.2	0.6 – 2.2
Concomitant use of medication other than for asthma					
No	858	31	1.0	1.0	
Yes	288	33	3.2	2.1	1.2 – 3.7

Table 7.2. Numbers of subjects with or without symptoms of clicking in TMJ in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	543	94	1.0	1.0	
35 or more	509	71	0.8	0.9	0.6 – 1.3
Gender					
Female	613	104	1.0	1.0	
Male	439	61	0.8	0.9	0.6 – 1.3
Smoking					
Never	493	76	1.0	1.0	
Stopped	266	46	1.1	1.1	0.7 – 1.6
Smoker	290	43	1.0	1.0	0.6 – 1.5
Alcohol					
Never	99	18	1.0	1.0	
Moderate	788	126	0.9	0.8	0.4 – 1.3
High	163	21	0.7	0.7	0.3 – 1.4
Residence					
Rural	128	23	1.0	1.0	
Urban	921	142	0.9	0.8	0.5 – 1.4
Education					
< 9 years	306	39	1.0	1.0	
9 years	359	73	1.6	1.5	0.9 – 2.5
12 years	386	53	1.1	1.0	0.5 – 1.7
Professional education					
Lower	507	76	1.0	1.0	
Upper	529	86	1.1	1.1	0.7 – 1.7
Concomitant use of medication other than for asthma					
No	783	106	1.0	1.0	
Yes	262	59	1.7	1.5	1.0 – 2.3

Table 8.2. Numbers of subjects with or without symptoms of toothache in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

Risk factor	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	577	60	1.0	1.0	
35 or more	529	51	0.9	0.9	0.5 – 1.4
Gender					
Female	656	61	1.0	1.0	
Male	450	50	1.2	1.2	0.8 – 1.8
Smoking					
Never	527	42	1.0	1.0	
Stopped	284	28	1.2	1.1	0.7 – 1.9
Smoker	292	41	1.8	1.6	1.0 – 2.6
Alcohol					
Never	103	14	1.0	1.0	
Moderate	838	76	0.7	0.6	0.3 – 1.1
High	164	20	0.9	0.8	0.3 – 1.6
Residence					
Rural	133	18	1.0	1.0	
Urban	970	93	0.7	0.7	0.4 – 1.2
Education					
< 9 years	317	28	1.0	1.0	
9 years	381	51	1.5	1.7	1.0 – 3.1
12 years	407	32	0.9	1.3	0.6 – 2.6
Professional education					
Lower	524	59	1.0	1.0	
Upper	565	50	0.8	0.8	0.5 – 1.4
Concomitant use of medication other than for asthma					
No	817	72	1.0	1.0	
Yes	283	38	1.5	1.5	1.0 – 2.5

Table 9.2. Numbers of subjects with or without sensitivity to hot, cold or sweet in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

Risk factor	Number of subjects		ORcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	637	215 (34)	1.0	1.0	
35 or more	580	174 (30)	0.8	0.8	0.6 – 1.1
Gender					
Female	717	262 (36)	1.0	1.0	
Male	500	127 (25)	0.6	0.6	0.4 – 0.8
Smoking					
Never	569	179 (32)	1.0	1.0	
Stopped	312	107 (34)	1.1	1.2	0.8 – 1.6
Smoker	333	103 (31)	1.0	1.0	0.7 – 1.3
Alcohol					
Never	117	44 (38)	1.0	1.0	
Moderate	914	293 (32)	0.8	0.7	0.5 – 1.1
High	184	51 (28)	0.6	0.7	0.4 – 1.1
Residence					
Rural	151	51 (34)	1.0	1.0	
Urban	1063	338 (32)	0.9	0.9	0.6 – 1.4
Education					
< 9 years	345	99 (29)	1.0	1.0	
9 years	432	154 (36)	1.4	1.5	1.0 – 2.1
12 years	439	136 (31)	1.1	1.3	0.8 – 2.0
Professional education					
Lower	583	196 (34)	1.0	1.0	
Upper	615	190 (31)	0.9	0.7	0.5 – 1.0
Concomitant use of medication other than for asthma					
No	889	267 (30)	1.0	1.0	
Yes	321	120(37)	1.4	1.4	1.0 – 1.8

Table 10.2. Numbers of subjects with or without bleeding from gums in different categories of potential confounders in Questionnaire Survey. Crude and adjusted odds ratios (OR) and 95% confidence interval for adjusted OR for independent variables when all potential confounders simultaneously retained in the model.

Risk factor	Number of subjects		Orcrude	ORadj	95%CI
	Without symptom	With symptom			
Age (years)					
< 35	637	248 (39)	1.0	1.0	
35 or more	580	186 (32)	0.7	0.8	0.6 – 1.1
Gender					
Female	717	244 (34)	1.0	1.0	
Male	500	190 (38)	1.2	1.2	0.9 – 1.5
Smoking					
Never	569	208 (37)	1.0	1.0	
Stopped	312	129 (41)	1.2	1.1	0.8 – 1.5
Smoker	333	96 (29)	0.7	0.6	0.4 – 0.8
Alcohol					
Never	117	34 (29)	1.0	1.0	
Moderate	914	325 (36)	1.4	1.3	0.8 – 2.0
High	184	73 (40)	1.6	1.6	1.0 – 2.8
Residence					
Rural	151	56 (37)	1.0	1.0	
Urban	1063	378 (36)	0.9	1.0	0.7 – 1.4
Education					
< 9 years	345	114 (33)	1.0	1.0	
9 years	432	165 (38)	1.2	1.2	0.8 – 1.7
12 years	439	155 (35)	1.1	1.1	0.7 – 1.6
Professional education					
Lower	583	216 (37)	1.0	1.0	
Upper	615	214 (35)	0.9	0.8	0.6 – 1.0
Concomitant use of medication other than for asthma					
No	889	314 (35)	1.0	1.0	
Yes	321	117 (36)	1.0	1.0	0.8 – 1.4