

A multidisciplinary study of patients with signs or symptoms attributed to dental restorative materials

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*The simple things are also the most extraordinary things,
and only the wise can see them.*

The Alchemist, Paulo Coelho

Dedicated to my sons Marcus and Simon

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Abstract

Background: Anxiety for adverse health effects caused by minute exposure to environmental chemicals has been described since the 1940s and has increased over the years. In Sweden, health problems associated with dental restorative materials, especially dental amalgam, have been discussed extensively off and on the last 30 years. The fear of mercury poisoning in combination with that the properties of the more esthetic materials have improved has caused some patients to exchange their amalgam fillings. The possible health effect of amalgam and health effect of replacements of amalgam have been extensively studied but the results are inconclusive. In Sweden, the use of dental amalgam has stopped since the use of mercury-containing products, among others in dental amalgam, was prohibited in 2009 for environmental reasons. There have been difficulties in verifying associations between the dental restorative materials and adverse reactions. The question of psychological influence on symptoms attributed to dental restorative materials has been raised and need further examination.

Aims: Describe the change in health for patients with symptoms attributed to their dental materials and to determine whether replacement of dental restorative materials had any impact on the perceived health. Furthermore, describe the personality, study self-image determine the level of psychological symptoms and the level of stress. Also evaluate regression of Lichenoid Contact Reactions and Oral Lichen Planus after replacement of the dental materials.

Methods: The study group consisted of 614 patients referred to the School of Dentistry, Umeå, Sweden with symptoms attributed to their dental materials. The examination at baseline included a clinical examination and a structured interview according to a predetermined protocol. At follow-up, a questionnaire was mailed to the patients that contained questions on among others; civil status, present health, medical and dental treatment, current employment situation and also a screening on psychological parameters. To evaluate personality the Swedish-item version of the Temperament and Character Inventory (TCI) was used in a group of patient with symptoms attributed to either electromagnetic fields or dental fillings. As a measure of self-image the introvert version of Structural Analysis of Social Behavior (SASB) was used, and the patients rated their psychological symptoms using Symptom Check List 90 (SCL -90). The group of patient with oral lichenoid lesion underwent a clinical examination both at baseline and follow-up and the questionnaire at follow-up contained the General Perceived Stress Questionnaire (PSQ), to measure stress during the past year.

Results Patients with complex symptoms had a more unfavorable long-term prognosis concerning remaining complaints than those with local symptoms only. The oral symptoms had decreased between baseline and follow-up and the general symptoms had increased. Furthermore, the results indicate that the patients might experience health improvement after removal of their dental restorative materials despite that the general symptoms have increased. The reason for this is unclear.

Concerning psychological parameters and personality the Electromagnetic Fields group scored significantly higher on persistence and the Dental fillings group scored significantly higher on Harm avoidance as well as psychosocially learned high Self-Directedness than the control group. Regarding self-image patients with Local Symptoms Only and Multi Symptoms scored significantly higher on “spontaneous” and “positive self-image” than the reference group. Furthermore, the level of psychological symptoms showed that the Multi Symptoms group scored significantly higher than the reference group but the Local Symptoms group did not differ from the references.

The remission of oral lesions after exchange of dental materials was seen to a greater extent in patients with Lichenoid Contact Reaction than in patients with Oral Lichen Planus. Furthermore, none of the patient showed any differences regarding psychological parameters.

Conclusion Symptoms attributed to dental restorative materials and/or electromagnetic fields seem to have multi-factorial causes where dental, medical, social, and psychological factors may be involved. Therefore, a multi-disciplinary approach is useful when examining the patients.

The patients showed personalities that could be vulnerable in the demanding modern society. This vulnerability can be expressed as various mental and somatic symptoms, which can be interpreted by the affected individual as attributed to either dental fillings or electromagnetic fields. Furthermore, the patients with Local Symptoms Only and Multi Symptoms showed a similar self-image, they were impulsive with an elevated positive self-image that can result in difficulties in setting limits and in combination with high demands, may result in mental stress. The level of psychological symptoms was higher in patients with Multi Symptoms showing that they were more psychologically stressed.

It was significantly more likely that Lichenoid Contact Reaction would regress after an exchange of dental materials than Oral Lichen Planus. Therefore, before an exchange of dental materials is commenced, a correct diagnosis of oral lichen is needed.

Papers in the thesis

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

- I Tillberg A, Berglund A, Mårell L, Bergdahl J, Eriksson N, Lindén G, Widman L. Changes in health over time in patients with symptoms allegedly caused by their dental restorative materials. *Community Dent Oral Epidemiol* (2005); 33(6): 427-437.
- II Bergdahl J, Mårell L, Bergdahl M, Perris H. Psychobiological personality dimensions in two environmental-illness patient groups. *Clin Oral Invest* 2005; 9: 251-6.
- III Mårell L, Bergdahl J, Tillberg A, Stenberg B, Berglund A. Psychological symptoms and self-image of patients with complaints attributed to dental restorative materials. (*in manuscript*)
- IV Mårell L, Tillberg A, Widman L, Bergdahl J, Berglund A. Replacement of dental restorations and oral lichenoid lesions. *J Oral Rehabil.* 2014 May;41(5):381-91.

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Introduction

Environmental intolerance

Anxiety for adverse health effects by very low-level of exposure to environmental chemicals has been described since the 1940s. Patients report general health complaints and some believe that the symptoms are caused by a very low exposure to environmental chemicals (1). The anxiety for exposure to environmental chemicals has increased over the years and for example effects of the exposure to “sick buildings” (2-4), electromagnetic fields (5-7), dental restorative materials, especially dental amalgam (8-10), and multiple chemical sensitivity (1, 11) have been discussed extensively. For patients with environmental intolerance the somatization pattern often changes over time and sometimes patients change their explanation for the cause of their illness from, for example, dental filling materials to electromagnetic fields (12). Polysymptomatic conditions are often observed in patients with environmental intolerance (12) and symptoms such as dizziness, fatigue, palpitations, headache and musculoskeletal pain in different parts of the body have been reported. Furthermore, problems with sleeping, concentration and lack of memory are common symptoms (13, 14). Complaints of oral symptoms such as dry mouth and burning mouth often result in consulting dentists (15, 16). Similar symptoms as in environmental intolerance (17) are found in other illnesses like stress related syndromes, for example in burnout syndrome (18). In a study of Anderberg (19) it was found that illness related to chronic stress is rather frequent and according to Ahola et al (20) the stress related burnout syndrome, is associated with three dimensions – mental disorders, physical illness as well as absence of sickness/disease.

However, in patients with environmental intolerance there has also been found physical illness as well as absence of sickness/disease. Regarding the definition of illness, disease and sickness there is a difference between them. Illness is defined as the ill health a person identifies himself or herself with, often based on self-reported mental or physical symptoms. Disease is

defined as a condition diagnosed by a physician or other medical experts. Sickness is related to the social role a person takes or is given in society, e.g. to be sick listed. These three concepts of illness, disease and sickness are often thought to overlap each other and a person who does not feel well, is diagnosed by a physician, and if the problem is serious and affect their ability to work, is sick listed (21) (figure 1).

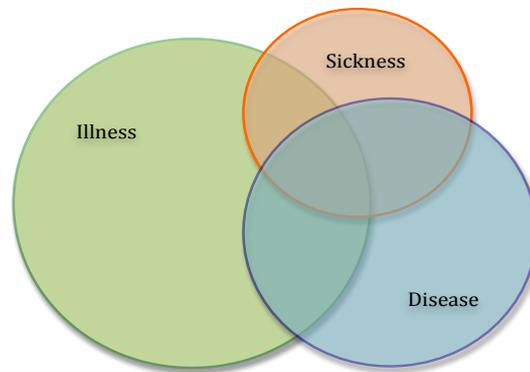


Figure 1. Relation between illness, disease and sickness respectively (21).

But, in reality things are not this simple, as some illnesses do not overlap the others and some diseases do not lead to sickness (21). For example if a person does not feel well, but can't be diagnosed with a disease, the person cannot be sicklisted despite the feeling of illness. That is often the problem for persons with environmental intolerance, since they cannot be diagnosed as having a disease. According to Wikman and Marklund women had a higher share in all three categories of morbidity (21). Furthermore, it is also known that about two thirds of patients visiting general practitioners are found not to have a biomedical disease, but still perceive themselves as ill (22). Patients with symptoms that do not correspond to biomedical findings, often called non-specific disorder or medically unexplained disorders, are primarily women (23). It has been found that women of all ages report more symptoms, take more medication and visit physicians more often than men (24). Among patients with environmental intolerance and general symptoms attributed to dental materials, the patients report illness but cannot be

diagnosed with a disease and consequently they cannot be sicklisted. About two thirds of these patients are women (25). Why women report more symptoms and illness is unknown.

The biopsychosocial model for explaining illness

Historically, physicians defined diseases in terms of somatic parameters. It was not necessary to be concerned of psychosocial issues, since it was outside the responsibility of medicine. Despite that, it was not possible to explain why some individuals experienced “illness conditions” when there were no positive laboratory findings to support the conditions. In the early 1970s, the American psychiatrist George Libman Engel claimed that psychological well-being play a protective role in the dynamic balance between health and disease and therefore proposed “The biopsychosocial model” (26). Engels suggested that the physician’s professional knowledge and skills must span the social, psychological and biological before decisions and actions are taken on the patient’s behalf, and health is best understood in terms of a combination of all these three (26). Engel highlighted the inadequacies and limitations of the traditional biomedical model and stated that the transposition from the narrow conceptual biomedical model to the biopsychosocial model was the major challenge for medicine in the seventies. In the 1990s Sparks proposed three major views in the explanation of environmental intolerance (6, 27, 28). One view was that it is a physical or psychophysiological reaction to multiple environmental chemicals. A second view was that symptoms may be precipitated by low-level environmental chemical exposures, but the underlying increased sensitivity may be initiated by psychological stress. A third view suggested that symptoms may be due to a misdiagnosed physical or psychological illness where a chemical exposure is not the cause of the symptoms (27, 28).

In Sweden health problems and illness associated with environmental intolerance and symptoms attributed to dental materials, especially dental amalgam, have been discussed extensively off and on the last 30 years. In recent years a possible exposure to bisGMA from dental composite restorations have been discussed (29).

Dental restorative materials

Since long ago man has sought durable and esthetic dental restorative materials, resulting in the use of many different materials for making artificial teeth as teeth are an important part of the facial structure and in most cultures they symbolize youth, health and beauty. There are more or less concerns about the toxicology of dental restorative materials and the debate regarding exposure to dental materials has increased over the years.

Dental amalgam has been used as a dental restorative material for over 180 years and is produced by mixing alloy powder with liquid mercury. It is difficult to establish when the use of silver amalgam began but it was in use in England in 1819, and 1836 the Frenchman August Taveau introduced silver amalgam on the continent. It was introduced into the USA in 1833 as "Royal Mineral Succedaneum" by the immigrant brothers Crawcour (30). Compared to gold, which was the main filling material at the time, the advantages of the new dental material were that it was much cheaper and quicker to insert (31-33). The material consisted of filings of silver coins mixed with an arbitrary amount of liquid mercury that hardened in the tooth during a large release of mercury vapor. From the very start, there were concerns regarding whether dental amalgam fillings were harmful to people (31-33). The American Society of Dental Surgeons banned the use of amalgam in 1841. There were several reasons for the ban – the large release of mercury but also the simplicity of the filling technique that made it possible for people without a dental education to fill teeth without any removal of carious tooth substance. In 1850 the ban of the use of dental amalgam was lifted but it has been controversial ever since, due to concerns about the potential health hazards. At the end of the 1890's GV Black systematized data on dental amalgam and set up guidelines for the content and the use of dental amalgam. Today, the main content of amalgam alloy powder is about 40-70% silver and about 20-30% tin, copper 5-30%, zinc 0-1%, but also a smaller amount of indium, palladium, or platinum.

In Sweden, reports of health problems attributed to dental amalgam have decreased from the 1980's and it is now a relatively small problem. But still, the fear of mercury poisoning is causing some patients to replace their amalgam fillings despite that research on toxic effects from mercury released from amalgam has failed to establish a causal relationship between the exposure and the symptoms presented by these patients (17, 34).

Resin-based composites represent one of the most important groups of dental restorative materials in dental practice today. Products with similar composition are also applied as pit and fissure sealants, luting composites and for crown build-ups and the bonding of brackets and orthodontic bands. Furthermore, resin-based composites are used for temporary crowns and bridges and most recently as root canal sealers. Resin-based filling composites are very complex mixtures containing many substances and are usually classified on the basis of: filler particles, matrix resin and coupling agents between fillers and matrix resins. Filler particles mainly consists of finely ground quartz, boron, silicate, lithium-aluminum silicate glasses and highly dispersed amorphous silicon dioxide. The matrix resin consist of a mixture of various monomers, for example Bis-GMA and/or UDMA, as well as various modifications of these molecules. More recent resin-based composites (ormocers) are based on a Si-O scaffold with methacrylic side chains, which are necessary for polymerization and Bisphenol A dimethacrylate (Bis-DMA) and ethoxylated Bis-DMA are used as comonomers. The coupling between filler particles and matrix resin is obtained through trifunctional alcoxy silanes, which are mostly called "silanes". Polymerization in products is mainly initiated by light, the light-sensitive initiator camphorquinone acts tighter with an aliphatic amine-type catalyst. Polymerization in autopolymerizing resin-based composite is strated by an aromatic amone/peroxide system, e.g., dimethylparatoluidine (DMP/benzoyl peroxide).

There are reports of health problems attributed to composite fillings and as late as in 2012 there was one study reporting impaired psychosocial function

in children with great exposure to bisGMA-based dental composite restorations (29).

Glass ionomer cement were introduced in 1972 by Wilson and Kent and are today used as filling material for cavity bases and buildups as well as for root canal fillings (ortograde/retrograde) and as luting agents for indirect restorations such as inlays, crowns and bridges. Glass ionomer cement adhere to both enamel and dentin and consists of powder and liquid systems. The powder contains finely ground glass (for example calcium and sodium fluorophosphoaluminosilicate) and the liquid typically consist of polyacrylic acid. The cement set through an acid-base reaction.

Resin-modified glass ionomer cements consist of a glass powder and a liquid composed of polymerizable groups attached to the polyacrylic acid and/or hydrophilic monomers. The cements are light-curable.

Dental ceramics comprise a comprehensive palette of different nonmetallic, inorganic materials. They are primarily used for inlays, veneers, partial crowns, full crowns and for coping. Oxide ceramics used in dentistry are primarily based on silicon oxide, aluminium oxide and zirconium oxide.

It is difficult to obtain dental materials that are completely inert and all these materials might release small amounts of substances, which in turn can cause side effects, such as allergic reactions. Thus, no matter what you put in the mouth the possibility of side effects cannot be excluded.

Side effects or adverse reactions of dental materials

A side-effects or adverse reaction is defined as an unintended and almost always negative reaction caused by a dental material when it is used according to the manufacturers recommendations. A prerequisite for an adverse reaction to occur is that the amount of substances released from the dental materials is large enough. The frequency of side effects to dental materials is considered to be low, compared to the vast number of dental treatments undertaken. Side effects, reported from dental personnel or

patients, can vary from objective reactions in the oral mucosa to more unspecific general symptoms (35).

However, adverse reactions can be subdivided into allergic reactions or non-allergic reactions with general or local toxicity, mechanical irritations or psychological impact (figure 2).

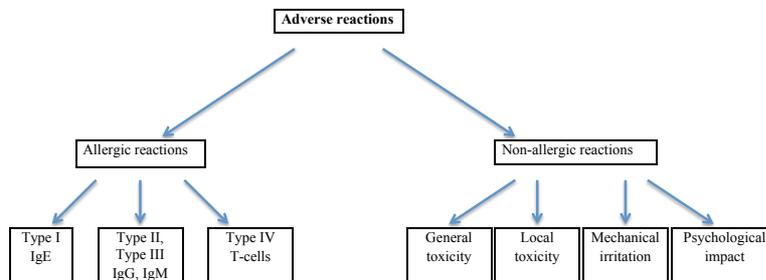


Figure 2. The adverse reaction might be caused either by an allergic reaction or toxicity, psychological impact or by a mechanical irritation.

Allergic reactions and non-allergic reactions

Almost all dental material release substances into the oral cavity, that can be transported with saliva and be swallowed or inhaled and thereby enter the human body with subsequent passage of the epithelial barriers in the gastrointestinal tract or the lungs and may via blood circulation be transported to different organs. The mechanism for this absorption depends on chemical properties of the released elements, whether they exist as particles, ions, as hydrophilic or lipophilic compounds, or as volatile substances (36). The non-allergic reaction and toxicity is supposed to be dose-dependent while the allergic reaction is usually not dose-dependent.

Allergic reactions

An allergic reaction is a strong immunologic reaction to a substance that usually represents no harm to humans. An allergic reaction could occur at

low concentrations of substances released from dental materials and a previous contact with immunologically active cells is a prerequisite (36). Allergic reactions can have immediate or delayed effects. An allergic reaction with immediate effects can be divided into three basic types (I, II and III) and are mediated by antibodies (IgE and IgG). The delayed type (IV) is mediated by T-cells (36). Type I is dependent on a genetic predisposition and Type II and Type III are not.

The most common adverse reactions from dental materials are Type I, IgE-mediated anaphylactic reactions, and even more frequent Type IV, T-cells mediated reactions, delayed-type hypersensitivity (36). The clinical manifestations of hypersensitivity in the mouth vary from symptoms such as burning mouth, pain and dryness of the mucosa to objective changes in form of nonspecific stomatitis and cheilitis with reddish, edematous mucosae erosions and ulcers (37).

Type I. Anaphylactic reactions, antibody-mediated

Immunoglobulin antibodies (IgE) bind to receptors on mast cells. Histamine is responsible for the visible symptoms of an allergic reaction such as running nose and tissue swelling. A severe type I allergic reaction may cause an obstruction of the respiratory system and a cardiovascular collapse.

Type II. Cytolytic or cytotoxic reactions

Immunoglobulins (IgM or IgG) bind to antigens on the surface of certain cells. The antigen-antibody complex activates the complement system and this activation may result in cytolysis, phagocytosis or chemotactic reactions.

Type III. Immune complex reactions

Complexes of antibodies (IgM and IgG) accumulate in blood vessels or tissues and activate the complement system, resulting in inflammation and vascular damage.

Type IV. Delayed-type hypersensitivity reactions

The allergic responses appear 12-24 hours after exposure, mediated by T-cells. Cytotoxin is released and macrophages are activated, which in turn cause local damage. Contact dermatitis (on the skin) is a common delayed allergic reaction that can be allergic (delayed reaction, cell mediated) or non-allergic (direct reaction).

Non-allergic reactions

General toxicity

A considerable number of single case reports published have claimed to present mainly chronic side effects of dental materials. However, the scientifically based literature reviews shows that causal relation between general health complaints and exposure to dental materials has very rarely been found. Furthermore, it has been concluded that there is no scientific evidence that dental amalgam could cause adverse reactions other than allergies. This conclusion was supported in publications by the Swedish National Board of Health and Welfare and the WHO (38-40).

Local toxicity and oral lesions

There are studies stating that there can be a local toxic effect of for example amalgam fillings as a result of the low-level mercury exposure in direct contact with the mucosa over several years (41). However, the most common reaction to dental amalgam is the development of oral lichenoid contact reactions (LCR), involving the mucosa in direct contact with amalgam restorations. A lichenoid contact reaction is a chronic lesion most often associated with long-term exposure of the oral mucosa to dental metals, but also acrylates and composite materials (42).

Oral lichenoid lesions are seen as reticular white patches, papules, plaques, erosions or ulcerations. The clinical appearance is similar to that found in oral lichen planus (OLP). The term "lichen planus" was first used in a

scientific publication in 1869 by the British dermatologist Erasmus Wilson and was by that time regarded as a rare affection of the skin (43). Later on lichen planus was considered to be a relatively common disorder affecting both the cutaneous tissues and the oral mucosa (44, 45) as many patients with skin lesions also have a mucosal involvement (46). Oral lichen planus (OLP) is supposed to be a chronic systemic disease with an immune-mediated pathogenesis (47) and recently it has been suggested that the mucosal lichen planus also should be considered as a chronic, immune-mediated, systemic disease (48).

By definition, lichenoid contact reactions (LCR) are limited to areas in frequent contact with restorations of dental amalgam or other dental materials, while Oral Lichen Planus (OLP) is an idiopathic disorder that also involves other regions of the oral mucosa. Lichenoid lesions or lichenoid contact reactions (LCR) resemble lichen planus both clinically and histopathologically (47). Oral Lichen Planus (OLP) exceeds the contact zone of the dental material or lacks contact with the restorations. Similarities in the reaction patterns on the cellular level preclude a differentiation between LCR and OLP, even if routine histopathology is supplemented by immunohistochemistry (49). Dunche et al. (50) concluded that an unambiguous distinction between OLP and LCR is not possible, neither clinically nor histologically. The reported prevalence of OLP in the population vary between 0.5-2.2 % (47), often with an onset beyond middle-age and more often in women than men (51). OLP is sometimes suggested to be a precancerous condition and the malignant transformation of OLP seems to vary between 0.5-2 % of the cases (52, 53), whereas no malignant progression of lichenoid contact reactions (LCR) adjacent to dental amalgam has been shown (50).

The etiologies of oral lichen lesions that have been suggested are among others autoimmune reactions, immunodeficiency, a genetic background, infectious agents, chronic liver disease, drugs, chemicals, stress, food allergies, diabetes, hypertension, malignant neoplasms, electrogalvanism as

well as dental materials (50, 54-56). It is well known that several drugs may cause adverse health effects and it has been found that some drugs may cause lichenoid reactions in the oral mucosa (57). Lichenoid drug reactions are seen as oral and/or cutaneous lesions that appear in connection with the intake of certain medications (47). There is limited and conflicting evidence that psychological factors, particularly acute stress and/or anxiety, contribute to the pathogenesis of oral lichen planus (54, 58, 59).

A clinical and histopathological definition of OLP was established by WHO (60), and a modified set of the WHO diagnostic criteria for OLP and oral lichenoid reactions was introduced in 2003 (61). The authors studied the correlation between clinical and histopathological assessment of OLP. They found a lack of agreement between the clinical and histopathological diagnosis, which means that it is impossible to rely on a clinical or a histopathological diagnosis alone. Furthermore, they stated that no distinction could be made between OLP and amalgam-associated or drug-induced lesions, either on clinical or histopathological grounds (61).

Oral chronic graft-versus-host disease (GVHD) is characterized by oral atrophy, erythema and lichenoid lesions and can only be seen after allogeneic bone marrow transplantation (62). GVHD has similar clinical and histopathological characteristics as OLP and LCR.

A higher prevalence of dental metal allergy has been found among patch-tested patients with OLP and LCR than in the general population, which indicates that an etiologic relationship exists (63). Positive reactions to mercury in patch tests are more frequently found among patients with lichenoid contact reactions (LCR) in contact with amalgam than in patients with an oral lichen planus (OLP) (64). Seventy percent of those with a strong topical association between their dental fillings and their mucosal lesions showed a positive patch test response to ammoniated mercury or amalgam. This was in contrast to those with a weak or no association between the lesions and their dental fillings where only 3.9% showed positive reactions.

In the general population the corresponding figure was 3.2% (64). Epicutaneous patch tests, however, seem to be of insignificant clinical value because patients with negative test results usually also show a regression of the lichenoid reactions after replacement of amalgam fillings in contact with the lesions (65).

Recent years research has shown that allergies to gold are also relatively common but it is no more common in patients with oral lichenoid lesions than in their matched controls (66, 67).

Mechanical irritations

In some patients oral lesions may be an oral manifestation of a chronic irritation induced by dental restorations. When old restorations are replaced, the new ones usually have smoother surfaces without sharp edges. This makes it difficult to determine whether a regression of a lesion is due to the exchange of the material in itself or if it is an effect of a smoother surface. In some patients, elimination of rough surfaces and sharp edges on the old fillings might led to regression of oral lesions (68). Even when oral lesions are not in direct contact with dental fillings, patients may experience recovery of local symptoms after removal of fillings. This could be due to parafunctions that may result in a contact between the lesions and the fillings (69).

Psychological impact

In most of the cases when patients are consulting physicians or dentists for adverse reactions and symptoms attributed to dental restorative materials a medical diagnosis explaining the patient's symptom cannot be found. It causes frustration and it also alerts insufficiency since many of the patients cannot accept a psychosomatic explanation of their illness and the consultation is often considered as disrespectful from the patients' point of view (70). Such conflicting encounters have been described especially when biological markers are absent and a precise location of bodily symptoms cannot be described (70, 71). Thus, it cannot be excluded that the

psychosomatic symptoms might be exacerbated by conflict-inducing sessions with dentists or physicians who reject the patient's explanation of the disorder.

There are studies on patients with symptoms attributed to dental materials, that suggest that the patients are more anxious, stressed and more depressed than their matched controls (72). There are also other studies that support the view of the syndrome as a psychosomatic disorder (73). Bågedal et al looked upon other factors than mercury release in these patients and the most striking result was the high prevalence of psychiatric disorders, nearly fifty percent had somatoform disorders, including "undifferentiated somatoform disorders". They also found that the patients reported more symptoms indicating mental illness than the controls (74). Sundström et al. (75) found that individuals with amalgam-related complaints reported more symptoms and had more negative life events than the controls. Furthermore, as an attempt to explain illness in patients with symptoms attributed to electromagnetic fields, it was suggested that a deviant self-image could result in stress-related symptoms and an increased psychosocial vulnerability (6).

Swedish National Board of Health and Welfare

The Swedish authorities have set up guidelines for the examination of patients with health problems suspected to be caused by dental amalgam. In 1988, 1991 and 1998 the Swedish National Board of Health and Welfare published general guidelines for both the dental and medical care of patients with symptoms attributed to dental restorative materials (38, 76, 77). Both dentists and general practitioners should examine the patients and it was concluded that there were no scientific evidence that dental amalgam could cause adverse reactions other than allergies. The conclusion was supported in publications by the Swedish National Board of Health and Welfare and by the WHO (38-40). Still patients with medically unexplained disorders and environmental intolerances are a clinical challenge. In the Netherlands as late as in 2011, there were published authorized guidelines for taking care of patients with Medically Unexplained Physical Symptoms (MUPS) and

Somatoform Disorders (SD) (78). Therefore, to achieve a better understanding, and to develop adequate treatments of patient with environmental intolerances and symptoms attributed to dental restorative materials there is a need of further evaluation of the psychological factors, simultaneously with an evaluation of both medical and odontological factors.

Nowadays, in Sweden, the use of mercury-containing products, among others dental amalgam, have been prohibited since 2009 for environmental reasons. New materials such as resin based materials have been introduced, partly to replace the mercury containing amalgam and partly because of esthetical reasons. But dental amalgam will still be present in people's mouths for the next 30-40 years. Adverse health effect of dental composite restorations has been reported. In the future there might be reports of new dental materials causing side effects unknown both to patients and dental personnel.

Aims of the study

- To describe the change in health for patients with symptoms attributed to dental materials and to determine whether replacement of dental restorative materials and follow-up time had any impact on the perceived health
- To describe personality in patients with symptoms attributed to either dental fillings or electromagnetic fields
- To determine the level of psychological symptoms and to study self-image in patients with symptoms attributed to their dental restorative materials
- To evaluate regression of Lichenoid Contact Reactions (LCR) and Oral Lichen Planus (OLP) after replacement of the dental restorative materials suspected to be the cause of the reactions.

Materials and methods

Study population and classification of the patients

The study population consisted of consecutive patients referred by dentists or physicians to the Department of Oral Diagnosis, School of Dentistry in Umeå, Sweden, for an examination of signs or symptoms attributed to their dental restorative materials. The examination at baseline included a clinical examination and a structured interview according to a predetermined protocol with questions regarding among others, civil status, present health, medical and dental treatment and other measures and precautions taken owing to the problems referred for. The inclusion criteria for participating in the study were that they at baseline should have stated that they believed that their dental restorative materials caused their symptoms, or that they had oral lesions that the referring dentist or physician suspected to be caused by the patients' dental materials. A total of 751 patients had been examined during the period but at follow-up initially 137 patients were excluded because of reasons such as missing or incomplete dental records (n=86), confirmed medical diagnosis that explained the symptoms (n=11), patients who had deceased between the first examination (baseline) and the follow-up (n=3) or patient that refused to participate (n=37) (figure 3).

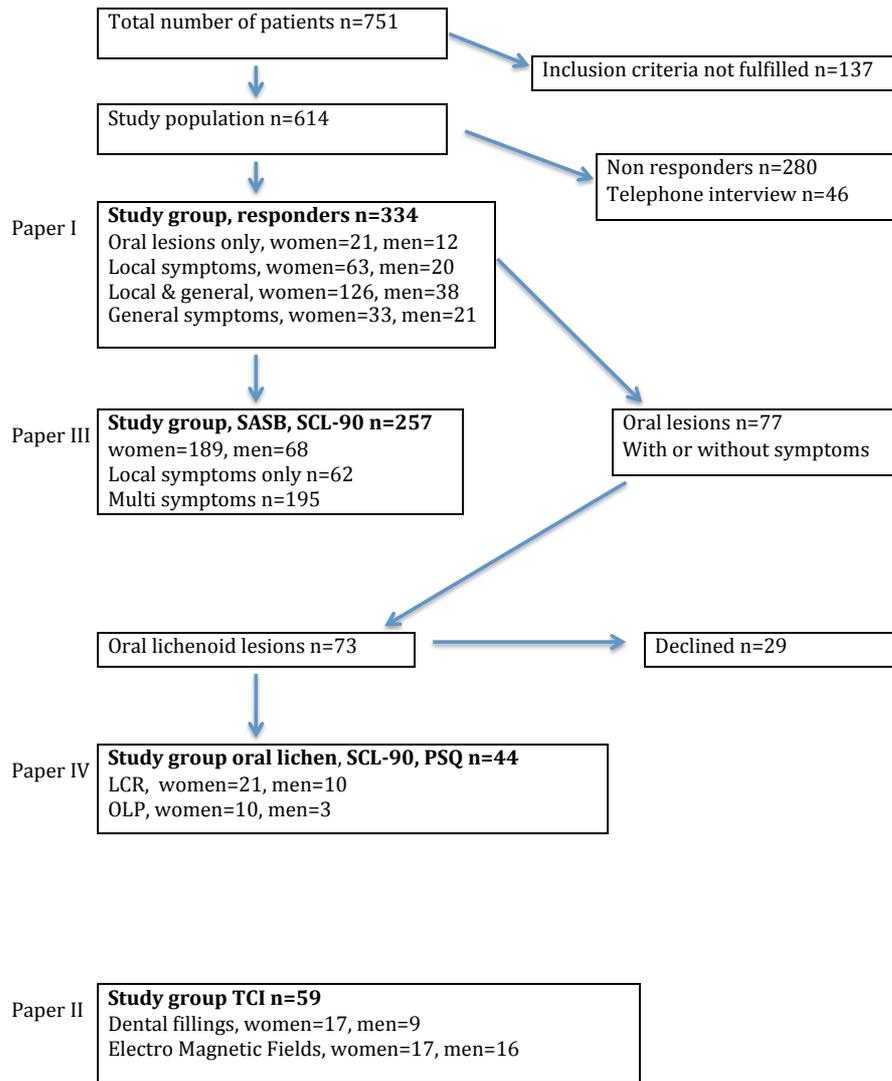


Figure 3. The study groups used for the follow-up.

Paper I, III and IV

At follow-up, a questionnaire was mailed to 614 patients and 334 (55%) were returned, forty-five patients returned more or less incomplete questionnaires together with a personal letter. Of the 334 patients, 73% were women and 27% were men, the mean age at follow-up for women was 57 yrs and 54 yrs for men. Regarding follow-up time, most of the patients (63%) had a follow-

up time between 3 and 6 years and the average follow-up time was 5.2 yrs. In paper I the classification of the patients in subgroups according to symptoms was performed from the baseline information in the dental records (figure 3). The most commonly reported symptoms were general problems, such as pain from joint and muscle, fatigue, vertigo and headache but also oral problems, such as burning mouth, dry mouth, taste disturbance and temporomandibular joints disorder (TMJ). The relative distribution between the subgroups 'oral lesions only', 'local symptoms only' and 'local and general symptoms', were not significantly different between the women and men. Patients with 'general symptoms only', however, were significantly more frequent among men ($p=0.04$).

Among the 334 patients who returned their questionnaires, there were 77 patients diagnosed having oral lesions such as oral lichen planus, oral lichenoid contact reaction and lingua geographica. All patients with oral lesions were excluded in paper III since oral lesions may be an explanation for perceived symptoms. The remaining 257 patients had oral or general symptoms that they at baseline had stated they believed were caused by their dental restorations. There were 74% women and 26% men with a mean age at follow-up of 55 yrs. In paper III the patients were classified into subgroups according to symptoms. One group with local symptoms only (LSO) ($n=62$, i.e. 24%) with a mean age of 62 yrs and one group with both local and general symptoms, multi-symptoms (M-S) ($n=195$, i.e. 76%) with a mean age of 54 yrs (figure 3).

Among the 77 patients who had oral lesions and were reached for a follow-up, 73 patients had received the diagnosis oral lichenoid reactions. Each of the 73 patients was invited to participate in a clinical examination and 44 patients accepted, the response rate was 60%. In paper IV patients with oral lichenoid lesions were divided into two groups, oral lichenoid contact reactions (LCR) and oral lichen planus (OLP), based on the baseline clinical examination and standardised colour pictures taken at baseline. The diagnosis was set according to modified WHO diagnostic criteria of oral

lichen planus (OLP) and oral lichenoid contact reactions (LCR) (47, 61). Patients with reactions in close contact with dental filling materials were diagnosed with LCR and the remaining patients, with reactions not topographically related to restorations, received the diagnosis of OLP. Of the patients, 70% (n = 31) were diagnosed with LCR, 21 women and 10 men, and 30% (n = 13), with OLP, 10 women and three men. Follow-up was an average 6 yrs after the first examination (figure 3).

Paper II

The patients in paper II were referred either to the Department of Psychiatry or the Department of Odontology, Oral Diagnosis, Umeå University and examined either by a psychologist or a dentist. All patients that were referred within a 4-year period and fulfilled the inclusion criteria were asked to participate. To be included in the study, the patients had to report symptoms that they assumed to be caused by either Dental Fillings (DF) or ElectroMagnetic Fields (EMF). When the patients (n=18) associated their symptoms to both DF and EMF, the primary source that they related their symptoms to was chosen as the main diagnosis. This gave a DF group of 26 patients, 17 women with a mean age of 50 yrs and nine men with a mean age of 48 yrs. The EMF group consisted of 33 patients, 17 women with a mean age of 47 yrs and 16 men with a mean age of 47 yrs (figure 3).

The study groups used in paper I, II, III and IV can be seen in figure 3.

Questionnaire

The questionnaire at follow-up was based on a version previously used in a project on health effects of Electricity and Visual Display Units and in the Office Illness Project in Northern Sweden (5, 79). The questionnaire contained questions on, among others, civil status, present health, medical and odontological treatment and other measures taken for the problems that the patients were referred for. Furthermore, consequences of the problems, precipitating factors, current employment situation, and questions

concerning self-image, psychological symptoms and perceived stress were included.

The psychological issues were evaluated with Structure Analysis of Social Behavior (SASB), Symptom Check List 90 (SCL-90) and General Perceived Stress Questionnaire (PSQ). Furthermore, The Swedish 238-item version of the Temperament and Character Inventory (TCI) was used to measure the personality.

Psychological parameters

Assessment of personality

The Swedish 238-item version of the Temperament and Character Inventory (TCI) (80-82) is a psychometric instrument designed to assess personality and is based on the general psychobiological model of personality developed by Cloninger (83). The psychobiological model divides the personality into a temperament and a character dimension. The temperament is considered to be mostly inherent and includes automatic emotional impulses, concrete operations and abstract deduction. The character, mostly psychosocially learned, includes intuition of basic cognitive schemas for organizing experience (81, 84) (figure 4). The TCI is a comprehensive inventory with broad clinical and scientific applications and is proven useful in diagnosis, differential diagnosis and treatment planning of mental disorders such as personality disorders (85). The Swedish version of the TCI has been validated, and normative data from a Swedish population are available, ranging from 20 to 80 years (86).

Temperament and Character Inventory (TCI)

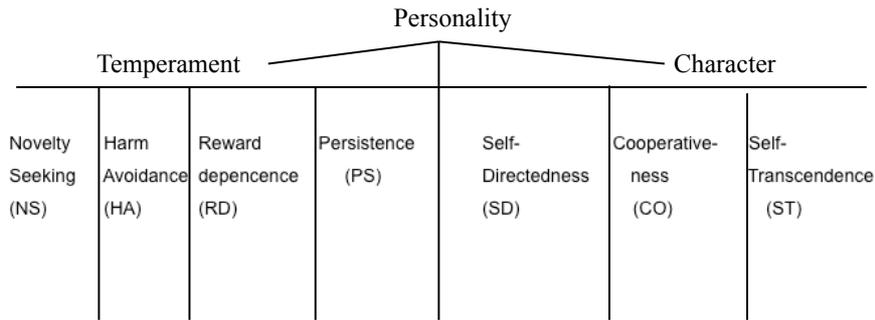


Figure 4. The Swedish 238-item version of the Temperament and Character Inventory (TCI). Model of personality (Cloninger et. al. 1994).

Assessment of self-image

Structural Analysis of Social Behaviour (SASB) was used to measure the self-image (87, 88). The SASB model is based on a social theory where personality is defined as how you treat yourself. The model consists of two basic dimensions; affiliation (love - hate) and interdependence (spontaneity – control). The two basic dimensions are formulated as statements rated on a scale between 0 and 100 describing how well the statement characterizes the person (figure 5). In this study, four clusters were assessed: spontaneous, controlled, positive and negative. The SASB-model has high test-retest reliability and internal consistency (87, 89, 90).

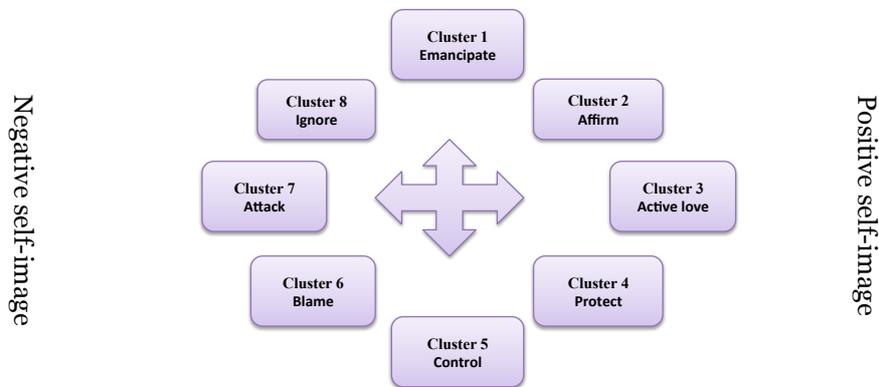


Figure 5. Self image; Structural Analysis of Social Behavior (SASB), cluster version.

Assessment of psychological symptoms

The Symptom Check List 90 (SCL -90) was administrated to assess psychological symptoms (91, 92). The SCL-90 consists of 90 items, scored from 0 (not at all) to 4 (extremely) and grouped into 9 different symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. The Global Severity Index (GSI), i.e. the mean of all 90 items, was used to measure the level of psychological symptoms. According to Derogatis (91) GSI is the best single indicator of the severity of disorder and should be used in most cases where a single summary measure is required. The SCL-90 has high internal consistency and high test-retest reliability (91, 92).

Assessment of stress

To measure the perceived general stress during the past month, the General Perceived Stress Questionnaire (PSQ) was used (93, 94). The PSQ emphasizes cognitive perceptions more than emotional states or specific life events and has been shown to be superior to alternative measures for predicting stress related diseases. The PSQ is a 30-item questionnaire and all items are scored from 1 to 4. A PSQ-index, varying from 0 (lowest level of perceived stress) to 1 (highest level of perceived stress), is derived from the total raw score using the formula: $(\text{raw score}-30)/90$. The PSQ has good reliability and validity and the factor analysis has revealed seven PSQ factors defining perceived stress: harassment, overload, irritability, lack of joy, fatigue, worries and tension (93).

Patch test

A patch test for hypersensitivity reactions to substances in dental materials was undertaken at baseline by an experienced dermatologist at the Department of Public Health and Clinical Medicine/Dermatology and Venereology, Umeå University for 31 of the 44 patients with oral lesions that fulfilled the criteria for patch testing. The dental screening series, as

recommended by the Swedish Contact Dermatitis Research Group, included 44 substances. The test substances were applied for 48 h, and readings were carried out on day 3 or 4, and day 7. Morphological evaluation was performed according to the international standard of the International Contact Dermatitis Research Group (95).

Reference group

An adult control population consisting of 2154 individuals was used to determine whether the patients in the study had significantly more symptoms than the general population. The reference group was a random sample of the Swedish population age 18–64 years, selected in 1998 by the Public Authority Statistics Sweden, Stockholm (96).

To evaluate the personality in the patient group, the controls consisted of 67 subjects (38 women and 29 men). To measure the self-image the controls consisted of 135 subjects, to measure psychological symptoms the controls consisted of 69 subjects and to measure perceived general stress the controls consisted of 418 subjects. The control groups were sex- and age-matched healthy subjects randomly selected from the database at the Department of Psychology, Umeå University, Sweden.

Drop out analysis

Of the 280 persons (45%) that did not return a completed questionnaire every sixth patient was contacted for a telephone interview. A total of 46 patients were interviewed and the most common reason for not responding was dissatisfaction with the questionnaire, especially with the psychological questions.

Of the 73 patients invited to the clinical examination of oral lesions (paper IV) twenty-nine individuals declined to participate and the most common

reason for not participating in the study was a lack of interest in controlling their lichenoid lesions.

Statistical methods

Comparisons between proportions were made using chi-square or Fisher's exact test. When comparing symptoms between baseline and follow-up and symptoms between the study population at follow-up and the reference population, the significance level was set to 0.01 because of multiple comparisons. In all other comparisons, the level was set to 0.05. The variables were tested using both univariate and multivariate logistic regression models in SPSS version 18.

Pearson's correlation coefficients were used to analyze the association between the TCI temperament and character dimensions. Comparing the DF-group and the EMF-group, Bonferroni test for corrections of multiple comparisons was used. Analysis of variance (ANOVA) was performed to compare the differences between men and women within the groups. P-values of less than 0.05 were considered significant. Statistical routines from the SPSS for Windows were used.

In order to compare the LSO, M-S and the reference groups, comparisons between proportions were made using chi-square test and the significance level was set to 0.05. Variations between means were tested by the Analysis of variance (ANOVA), and with Bonferroni test for corrections of multiple comparisons. All analyses were conducted using SPSS 20 for Macintosh.

Differences between LCR and OLP groups regarding the regression of oral lichenoid lesions, classified as regressed or not regressed, were analyzed using the chi-square test. Differences regarding the regression of the lesions between the patients in the LCR group with no, partial or total exchange of suspected materials were analyzed using the chi-square test. Differences regarding the regression of lesions after an exchange of dental materials

were compared between the LCR patients with positive and negative patch test reactions to dental materials using the chi-square test. The significance level was set to 0.05. Finally, differences between the two groups and a reference group regarding the psychological parameters The Global Severity Index (GSI) and the General Perceived Stress Questionnaire (PSQ) were analysed using the Analysis of variance (ANOVA), with Bonferroni test for corrections of multiple comparisons. The significance level was set to 0.05. All analyses were conducted using SPSS 22 for Macintosh.

All studies were approved by the Ethics Committee of Umeå University, Umeå, Sweden.

Results and discussion

Fact box

Patient referred from: Dental and Medical Health Care professionals from the counties of Västerbotten, Norrbotten and Västernorrland
Diseases prior to baseline examination: Diseases of importance for the patients' symptoms
Baseline variables: Sex, age, marital status, No. of children, education, type of work
Oral lesions: Oral lichenoid contact reactions (LCR) and oral lichen planus (OLP)
Hypersensitivity reactions: Patients with oral lesions that fulfilled the criteria for patch testing.
Oral symptoms: Burning mouth, dry mouth, increased salivation, taste disorder, TMJ pain, stiffness/numbness
General symptoms: Fatigue, headache, nausea, anxiety, depression, sleeping problems, vertigo, eye symptoms, skin symptoms, circulatory symptoms, muscular and joint problems
Remaining oral and general symptoms at follow-up: Symptoms remain unchanged, almost unchanged, remained to a limited extent or symptoms disappeared
Replacement of dental restorative materials: Total, partial or no replacement of dental materials
SASB: Structural Analysis of Social Behavior to measure self-image
SCL-90: Symptom Check-list to assess psychological symptoms
PSQ: General Perceived Stress Questionnaire to measure the perceived general stress during the past year
TCI: Temperament and Character Inventory to assess personality dimensions

Many of the patients referred to "Utredningsenheten" Department of Oral Diagnosis, School of Dentistry in Umeå for symptoms attributed to dental restorative materials were dissatisfied, suspicious and critical since they believed that their complaints were caused by incorrect treatment with dangerous dental restorative materials and they claimed that their health problems were not taken seriously neither from the dental care nor the health care professionals. Therefore it was of great interest in this study to determine whether our patients had more symptoms than the general

population or whether they got health improvements after the exchange of dental materials. Furthermore, to examine the personality and determine if our patients have more psychological symptoms, are more anxious, stressed or depressed than controls. Comparison was also made with the subgroup of patient with the most common reaction to dental restorative materials, oral lichenoid lesions.

Baseline characteristics of the study group

The whole study group (n=334) reported both oral and general symptoms at baseline, described in the patients' dental records. Burning mouth was the most frequently reported complaint followed by dry mouth and taste disorder. The most common general symptoms reported were fatigue, headache, muscular problems, and joint problems (figure 6). Some patients also attributed their symptoms to sick buildings (3%), visual display units (3%) and hypersensitivity to electricity (5%) (table 1).

The group of patients with oral lesions, Oral Lichen Planus and Lichenoid Contact Reaction also reported both oral and general symptoms at baseline. The most common oral symptoms reported were burning mouth followed of dry mouth, and taste disorder. The most common general symptoms were fatigue, headache, muscular problems and joint problems (figure 7).

Changes of symptoms after replacement of dental materials

Replacement of dental materials

The most frequently replaced material was dental amalgam. The choice of replacement materials was often a mixture of materials, e.g. metal ceramic crowns in noble alloys in the molar region and filling materials such as composite or glass ionomer in the canines and premolars.

Among all patients in the study group, 76% had carried out a partial or a total replacement of dental restorative materials that was believed to cause their symptoms. Replacement of dental materials was more common among patients with multi-symptoms compared to patients with local symptoms or

patient with oral lesions ($p=0.03$). There was no significant difference between women and men.

Despite the recommendations to the patients with oral lichen, many of them had exchanged all their suspected fillings with an alternative material, even if there was no contact between the filling material and the oral lesion. Of the 44 patients with oral lichen, 52% had replaced all their dental restorations and 36% had done a partial replacement. The remaining 12% of patients had not exchanged any of their restorative materials, although they were recommended to do so.

Oral symptoms at follow-up

The patients in the whole study group reported a decrease of the symptom burning mouth from baseline to follow-up. Burning mouth among women had decreased significantly ($p<0.01$), while the decrease among men did not reach significance ($p=0.02$). Most of the patients had replaced their suspected dental materials, which in turn could have resulted in a decrease in the symptom burning mouth. The symptom dry mouth was reported to the same extent among women while men reported an improvement of dry mouth despite they had been older and/or could have got more medication. Taste disorder was significantly reduced ($p=<0.01$) for both women and men (figure 6).

Burning mouth has been found to be a common symptom in connection with dry mouth (97) and is also a common symptom in patients with oral lichenoid lesions, especially for patients with the atrophic-erosive type of lichen (98). In this study the patients with lichenoid contact reactions (LCR) and oral lichen planus (OLP) reported that the symptom burning mouth had decreased significantly ($p=0.03$) from baseline to follow-up. However, statistically we found no significant correlation between lichenoid lesions and burning mouth, neither at baseline nor at follow-up. Furthermore, no significant correlation that an exchange of dental materials affect the symptom burning mouth. Despite that there was no significant correlation between burning mouth and exchange of dental materials, the patients' self-

assessed symptoms had decreased after removal of the dental filling materials, especially amalgam, and the patients declared that they felt better after replacing their dental restorations with other dental materials. A reasonable cause to the decrease of burning mouth symptoms could be that all patients with positive epicutaneous test had exchange dental materials or avoided all allergens. It is difficult to draw any firm conclusions since the groups are limited. The contradictory results in this study may be dependent on the small groups in both the OLP-and the LCR-group.

The complaints of dry mouth had increased significantly ($p=0.01$) from baseline to follow-up. The increase of the symptom dry mouth at follow-up seems reasonable because the mean age had increased from 56 to 62 years and the patients may have received more medication that might in turn have give reduced salivation. Furthermore, a larger part of the patients were women, 70%, and dry mouth is a frequent effect of menopause (99, 100). Taste disturbances had also increased significantly ($p=0.00$) between baseline and follow-up (figure 7).

General symptoms at follow -up

In the whole study group the frequency of the majority of general symptoms increased significantly between baseline and follow-up for both men and women. Fatigue, difficulties in concentrating, eye irritation, dry eyes, nasal symptoms, cough, hoarseness, and the sensation of a lump in the throat increased significantly ($p<0.01$) among women. Skin problems, dry facial skin, facial erythema, facial sensory, symptoms and body itchiness had increased significantly ($p<0.01$) for women. However, joint pain was the only general symptom that decreased significantly ($p<0.01$) for men between baseline and follow-up, and it was reduced by almost half. Some of the reported general symptoms can be seen in figure 6.

The patients with lichenoid contact reactions (LCR) and oral lichen planus (OLP) also reported general symptoms and there were a significant increase of the symptom fatigue ($p=0.01$) and of muscular problems ($p=0.00$) from

baseline to follow-up while headache ($p=0.05$) and joints problem ($p=0.00$) decreased significantly (figure 7).

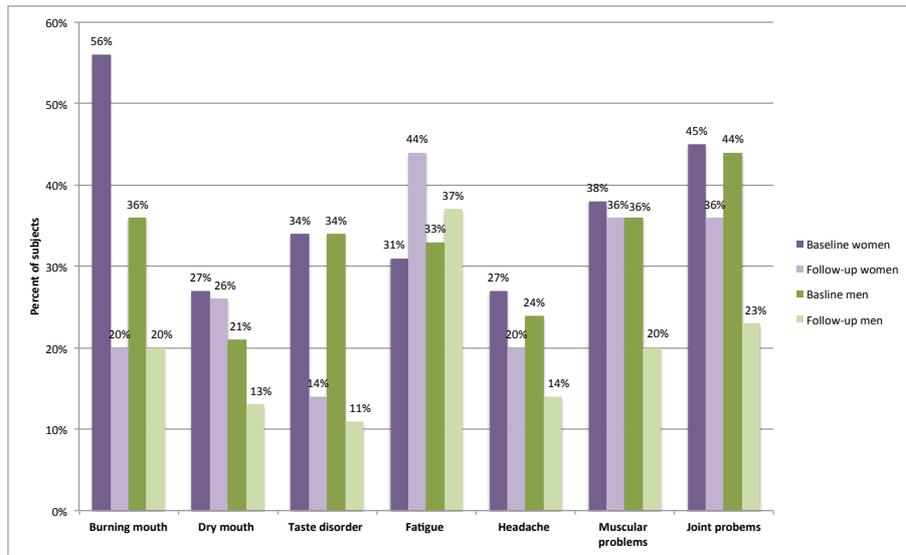


Figure 6. Distribution of oral and general symptoms in the study group at baseline and at follow-up.

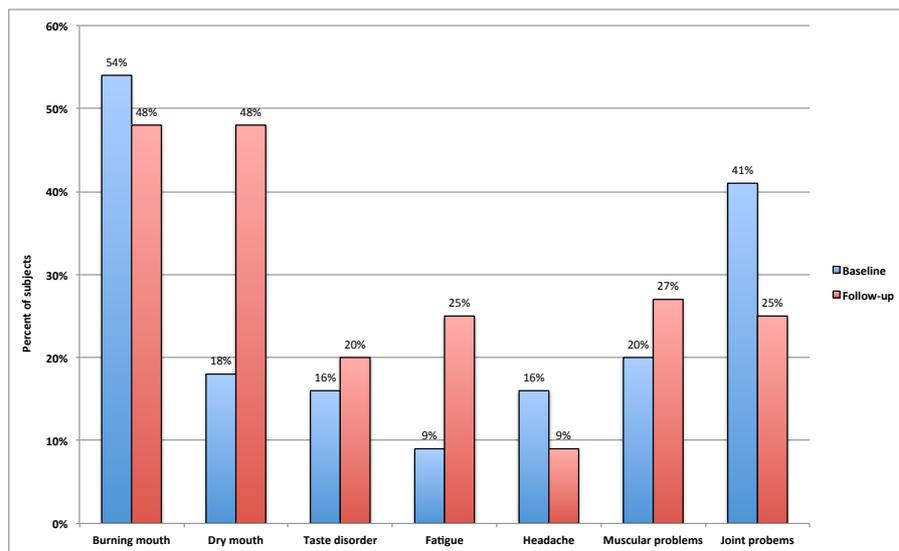


Figure 7. Distribution of oral and general symptoms in the groups with OLP and LCR at baseline and at follow-up.

The prevalence of symptoms at follow-up in the patient group was significant higher ($p < 0.01$) compared to a Swedish reference population (figure 8).

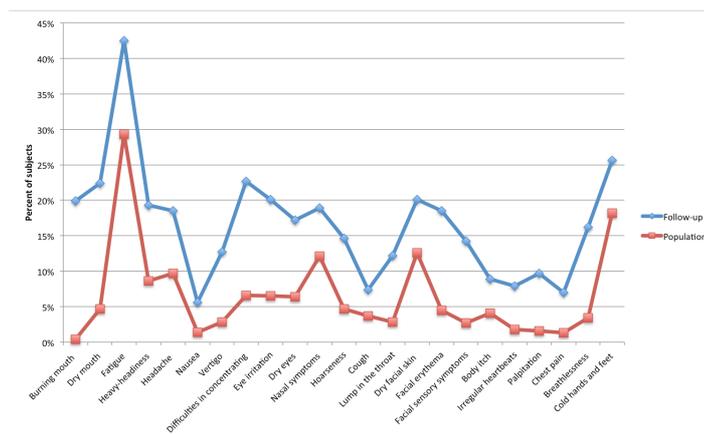


Figure 8. Symptoms in the study group at follow-up in comparison with a Swedish reference population.

The distribution of symptoms at follow-up is for the study group and the subgroup is listed in Table 1.

Table 1. Symptoms at follow-up reported by the examined groups (valid present).

	Study group (n=334)	Oral lichenoid lesions (n=44)
Burning mouth	20	48
Dry mouth	22	48
Taste disorder	13	20
Fatigue	42	25
Muscular problems	32	9
Joint problems	33	27
Sick buildings	3	-
Visual display units	3	-
Hypersensitivity to electricity	5	-

Health improvements

Patients experienced health improvements after removal of their suspected dental materials and the oral symptoms had decreased between baseline and follow-up. However, the general symptoms had increased between baseline and follow-up and despite that they still experience health improvements, both men and women, which is a contradictory result.

In connection with replacement of dental restorations, 14 % of the patients reported relief from symptoms. Patient that had replaced their restorations completely perceived a significantly larger alleviation ($p > 0.01$) of their symptoms compared to the others but a total replacement of dental restorative materials had no significant impact on the ability to recover completely (table 2). Furthermore, patients with complex symptoms had a more unfavorable long-term prognosis concerning persistent complaints than those with local symptoms only ($p < 0.05$). The risk of having any remaining complaints was more frequent among men. There was a significant difference between women and men regarding the perceived alleviation of symptoms in connection with replacement of dental materials, 43% for men and 64% for women ($p = 0.006$). “No effect” after replacement was reported of 37% men, whereas the corresponding figure for women was 19%.

However, in patients with medically unexplained disorders it has been shown that treatment such as psychophysiologic interventions usually are better accepted than psychotherapeutic interventions (101). Katsamanis et al. (101) showed that a “medicalized” treatment is better accepted than psychotherapeutic interventions and the reason can be that the patients tend to think that the problem is in the body and not in the mind, despite the lack of biomedical signs. The possible effect of placebo has also been discussed since many patient report health improvements and decrease in symptoms after treatment with exchange of dental materials (102).

Table 2. Replacement of dental restorations and perceived health at follow-up, stratified for gender.

	Total group		Women		Men		<i>p-value</i>
	%	n	%	n	%	n	
Complete replacement of restorations	40.6	121	42.1	90	36.9	26	0.42
Partial replacement of restorations	36.2	108	36.4	78	35.7	25	0.90
No replacement of restorations	23.2	69	21.5	46	27.4	22	0.28
Reactions after replacement	52.0	119	54.2	91	45.9	28	0.27
No reactions after replacement	48.0	110	45.8	77	54.1	33	0.27
Symptoms at follow-up:							
Unchanged	19.1	62	17.5	41	23.3	21	0.23
Almost unchanged	25.1	81	22.6	53	31.1	28	0.12
Remained to a limited extent	37.3	121	41.5	97	26.7	24	0.02
Disappeared	18.5	60	18.4	43	18.9	17	0.92

The patients with oral lichenoid contact reactions (LCR) and oral lichen planus (OLP) were asked if they experienced health improvements after removal of their suspected dental materials. Since the estimate from one patient in the LCR-group is missing there were 43 answers. There were 34 patients that felt better or had no symptoms while no effect of the replacement was reported by seven patients. Two patients in the LCR-group stated that they had got worse after replacement of fillings and one patient in the OLP-group felt better despite no exchange of dental filling materials (table 3).

Table 3. Self-assessed effects after replacement of dental materials in the OLP-group and the LCR-group.

	Total exchange		Partial exchange		No exchange	
	LCR (n=14)	OLP (n=9)	LCR (n=13)	OLP (n=3)	LCR (n=3)	OLP (n=1)
Worse	0	0	2	0	0	0
No effect	1	2	1	0	3	0
Better	7	3	7	2	0	1
Symptom-free	6	4	3	1	0	0

Studies on patients attributing their symptoms to dental restorative materials have reported a various number of both local and general symptoms (49, 103-105). Several studies have been published regarding the effect of removal of amalgam restorations on the general health and the results are not consistent (25, 106-108). Improvement of symptoms were reported after removal of dental fillings, mainly amalgam, but the symptoms were not reduced to the level of a general population (106), which is in accordance with our findings.

However, in the present study many patients reported that their health had improved after the replacement of their dental restorations, but this improvement was only significant for oral symptoms, which is in accordance with a Norwegian studies of Lygre et al. (107, 108). In patients with complex general symptoms no improvement was found, on the contrary these symptoms had increased between baseline and follow-up for both men and women.

It is contradictory that the majority of reported general symptoms had increased, while the patients perceived that their health had improved. However, the reason for this improvement is unclear.

Regression of oral lichenoid lesions

The patients with oral lichenoid lesions were divided into two groups according to Al Hashimi et al (47), oral lichenoid contact reactions (LCR) and oral lichen planus (OLP). At follow-up, remission was seen in 71% (n=22) of patients with LCR and in 8% (n=1) of patients with OLP and the difference was significant ($p= 0.000$) (figure 9).

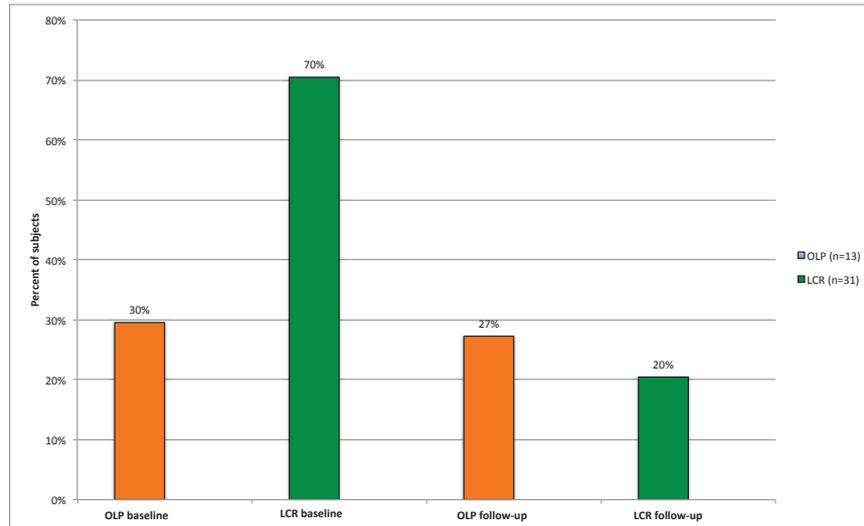


Figure 9. Remaining oral lichenoid lesions at follow-up.

In the OLP-group, one patient showed a complete remission of the oral lesions and this patient was the only one that had not replaced any dental materials. The remaining 12 patients (92%) had undergone a partial or a total replacement and still had their oral lesions (table 4).

Table 4. Replacement of dental restorations and remission of oral lesions at follow-up.

	No exchange (n= 5)		Partial exchange (n= 16)		Total exchange (n= 23)	
	Healed	Not healed	Healed	Not healed	Healed	Not healed
OLP (n=13)	1	0	0	3	0	9
LCR (n=31)	3	1	7	6	12	2
Total	4	1	7	9	12	11

The lesions regressed significantly more often ($p=0.00$) in the group of patient with LCR (71%) compared to the group with OLP (8%). This is also a reasonable outcome because OLP is suggested to be an immunemediated condition, while LCR is caused or affected by extrinsic factors. The results in

the present study are in accordance with the results in other studies (109). Furthermore it has also been reported that lesions in close contact with dental restorations regress to a greater extent than lesions without contact (110) and even when lichenoid lesions are not in direct contact with amalgam, patients may experience recovery of local symptoms after removal of amalgam fillings which can be due to removal of rough surfaces or sharp edges of dental restorations. In this study it was not possible to determine whether a regression was more frequent when using a certain replacement material because the replaced materials were often a mixture of materials.

Spontaneous total remissions of LCR occurring without removal or replacement of suspected filling materials has also been reported (111). In this study there were three patients in the LCR group whose lesions regressed without any exchange of materials and the only OLP patient whose lesion regressed, did not exchange any dental materials.

Despite an exchange of all restorations in the patients with OLP, their lesions did not regress.

Hypersensitivity reactions

At baseline, 31 of the 44 patients (70%) were patch-tested with the dental screening series and 18 (58%) showed positive reactions, 12 patients with LCR and 6 patients with OLP (Figure 10).

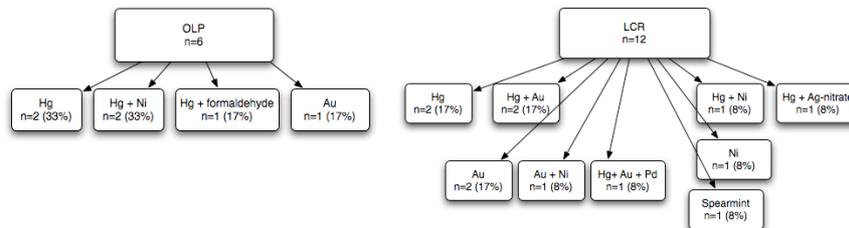


Figure 10. The 18 patients with positive patch test reactions to the dental screening series – (OLP) (n=6) and (LCR) (n=12). The elements that the patients showed positive reactions to are given with the number and percentage of patients that showed these positive reactions.

In the OLP-group the most frequently identified allergens were mercury (83%, 5/6), nickel (33%, 2/6) and gold (17%, 1/6) (figure 10). However, no remissions of the lesions were seen after the removal of dental amalgam fillings in this group despite an exchange of all restorations in patients with a positive patch test to both mercury and gold. This supports the assumption that exchange of restorations in patients with OLP does not affect the lesions and that the mucosal lesions were probably not caused by contact reactions to their dental materials.

In the LCR-group the most frequent allergens found were also mercury (58%, 7/12) and gold (50%, 6/12), followed by nickel (25%, 3/12) (figure 6). Eleven of the 12 patients had partially or totally exchanged their restorations, and nine patients (75%) showed total remission of their lesions. There were seven LCR patients with positive reactions to mercury and all lesions regressed after a total replacement of amalgams. Among the 20 patients that had been patch-tested in the LCR group, there was no significant difference in the regression of lesions between the patients with positive and negative patch test results after an exchange of materials.

The value of patch tests as a predictor for the effect of an exchange of dental restorations on lichenoid lesions has been discussed. Thornhill and co-workers suggested that positive patch test reactions to mercury are more frequently found among patients with lichenoid reactions in contact with amalgam than in patients with OLP (64). However, a recent review concluded that patch tests are of limited value as an indicator for predicting the effect of replacement of amalgam filling on lichenoid lesions (41), since dental amalgam may cause lichenoid contact reactions without an allergic reaction.

With regard to positive epicutaneous patch test reactions and exchange of dental materials, the present study showed that lesion remission was greatest among patients with LCR and positive dental screening patch tests and a total replacement of dental materials (n=8). Positive patch test results

were also found in OLP-patients (n=6) and despite an exchange of all restorations their lesions did not regress.

Lichenoid contact reactions can also occur in close topical relation with composite resins. Currently, it is not known whether these reactions are induced by a delayed hypersensitivity to formaldehyde or if they represent a topical adverse reaction associated with resin components (68). One patient in the OLP-group, had a positive patch test reaction to both formaldehyde and mercury, and although the patient both exchanged amalgams and composites, the lesions did not regress. So, the mucosal lesions were probably not caused by contact reactions to the dental materials. The patch test had no prognostic value for these patients with OLP.

It has been found that oral lichen is more frequently seen in women (47) and this is also in agreement with the results of the present study where the study group with oral lesions consisted of 31 women (70%) and 13 men (30%).

Environmental intolerance

When patients are consulting physicians and dentists for symptoms attributed to environmental intolerance and symptoms attributed to dental restorative materials, and neither the dentists nor the physicians can find a medical diagnosis explaining the patient's symptoms, it will cause frustration for both the patients and the caregivers. Depending on the approach of the medical and dental care providers, the consultation can be perceived as disrespectful by the patient and they may feel dismissed by the doctor (70, 71). The patients are convinced that environmental factors such as dental amalgam or electromagnetic fields made them sick and they will not accept a psychosomatic explanation of illness. Many of the patients feel that they have been rejected as malingerers by doctors or dentists. Similar experiences in the consulting situation have been described among patients with musculoskeletal pain (112), chronic fatigue syndrome (113), orofacial pain (114), and fibromyalgia (115). They feel as if their own explanation of the

factors causing illness is rejected by the health care. These patients experience themselves as being victims of an unknown disease and consider themselves misjudged by doctors and dentists when they are not given a physical explanation for their symptoms (112-114).

When patients feel misjudged of the health care system, they often search for help from alternative medicine and especially patients with symptoms attributed to environmental intolerance often find more support and confirmation from caregivers from the alternative medicine. Clearly, alternative medicine has a broader and a more vague definition of disease; if you feel ill, choose to be ill or have an illness behavior, then you have a disease (116). In alternative medicine, the definition of illness, disease and sickness (figure 1) overlap to a greater extent than that in biomedical science, and this gives alternative medicine a great advantage to explain illness (116). It has been found that patients commonly combine alternative healing systems to provide alternative explanations of illness, while simultaneously using conventional health care (117).

However, an explanation from the alternative care is not accepted as a basis for a diagnosis or for providing a sick-leave certificate. Therefore, the patient has to consult medical care for new examinations, which can give rise to a cycle in medical and dental care that may even exacerbate the symptoms. A medical diagnosis from a doctor provides access to welfare benefits such as sick-leave certificates or disability pensions (115). This makes it understandable why a diagnosis is extremely important for the patient (112).

In an attempt to interrupt these behaviors of numerous consultations, the model by Wikman and Marklund (21) may be helpful (figure 1), and can be used as a basis for discussion with patients. The patients can understand that their experiences are situated in a different part of the model than the one which allows diagnoses, and that their experiences are not questioned and also that they are not to blame for the knowledge gap. This could create trust in the encounter and a base for recovery. Definitions of illness, disease and

sickness and what they represent are not either immutable, but changes over time (116).

Patients with symptoms that do not correspond with biomedical findings, medically unexplained disorders, are most often women (23). Also among patients consulting for environmental intolerance and symptoms attributed to dental materials, women represent about two thirds (25). Furthermore, it is known that women at all ages report more symptoms, take more drugs and visit physicians more often than men (24).

This is in agreement with the results of the present study of patients with symptoms attributed to dental materials or electromagnetic fields. The study group (n=614) consisted of 71% women (n=436) and 29% men (n=178). Furthermore, according to the questionnaire, nearly all symptoms were more prevalent among women than men. Oral symptoms were more prevalent in women, except for burning mouth, which was evenly distributed between women and men. However, burning mouth was more common among women than men both in the whole study group but also among the patient with oral lichenoid lesions.

There was also a difference between women and men regarding perceived alleviation of symptoms, where women reported a larger perceived alleviation of symptoms than men. However, the difference was only significant for symptoms 'remaining to a limited extent', where the proportion of women was almost 60% larger than that of men.

Bio-psychosocial health model

The relationship between body and soul has been known for many years although there has still not been a breakthrough within medicine. The reason for this can be that the biomedical paradigm is predominating the health care and the dental care. The biomedical approach is that diseases only can be defined by measurable biological variables and therefore no space is provided for social, psychological or behavioral dimensions of ill health (26). Although, investigations on health-care consulting and experience of illness

have demonstrated that whether or not people became incapacitated as a result of illness is determined not only by the specific physical signs, but also by psychological and social factors (118). So, despite the success with the biomedical research the psychological and social aspects have been neglected.

Already in the seventies Engel (26) suggested that the body, the patients personal history, life experiences and the current social circumstances play a role in the pathogenesis of illness and in the patient's interpretation of their symptoms. Furthermore, Engel claimed that all this matters in the presentation of illness and he called the model for "The Biopsychosocial model". Main et al (118) concluded that it is essential to treat the whole person within the context of their disease rather than simply treating the signs and symptoms of their disease. The Biopsychosocial model is required to explain the persistence of illness-related disability (118). It is known that exposure to stress factors may often determine the onset of many illnesses, although the relationships are highly complex. Furthermore, it is also known that stress factors are very important in the etiology of diseases and both psychiatric and somatic disorders are affected by long-lasting exposure to negative stress (119, 120).

Bratel et al. (49) found that there was a high frequency of reported earlier negative life events in patients with symptoms attributed to dental fillings, which also was found by Langworth et al (25). Similar results were reported in a more recent study of Sundström et al. (121), where it was shown that many patients with amalgam-related complaints had experienced negative life events before and at the onset of the complaints. The conclusion was that they had not been able to handle the traumatic events adequately and therefore developed somatic reactions (121).

Studies have shown that a considerable part of patients, 30 % in primary health care and 15 % in district dental clinics, have reported complex psychosomatic problems which means that general physicians and dentists

meet these patients on a regularly basis (122). It is reasonable to assume that the modern dental care should include education about psychosomatics, psychology and sociology (123), which will enable the dentists to apply a biopsychosocial approach. Therefore we have to question the bio-medical paradigm and replace it with a bio-psychosocial approach that give us possibilities to consider all aspect of ill health and disease (124).

Psychological parameters

In an attempt to look at other factors of adverse reactions to dental materials than replacement of dental restorations, symptoms, mercury release or regression of oral lesions in this patient group we decided to have a more bio-psychosocial approach and also examined the patients with a more psychological approach. We decided to evaluate personality, self-image and psychological symptoms and in the group of patients with oral lichenoid lesion we measured stress during the past year.

Personality

To investigate the personality of patients with sensitivity to either dental fillings (DF) or electromagnetic fields (EMF), the Swedish 238-item Temperament and Character Inventory (TCI) (80-83) was used. The TCI divides the personality into a Temperament dimension, which is considered to be heritable and manifested in early life (80) and a Character dimension, which is defined in terms of aspects of self-concept (82). The personality is defined as an interaction of these two (80) (figure 4).

The results showed that the EMF-group scored significantly higher in the inherent Temperament dimension Persistence (P) compared to a control group. They can be described as industrious, hard working and stable despite fatigue. Furthermore, eager to start work on any assigned duty and tend to perceive frustration and fatigue as a personal challenge. Thus highly persistent individuals tend to be perfectionists who push themselves far beyond what is necessary (125). Rapid changes, both in working and private

lives, can be a challenge for individuals with high persistence to adjust to or adapt to. In turn, this may result in various symptoms, especially stress-related symptoms, and the patients therefore may tend to blame external factors such as electricity to cause their symptoms (table 5). No differences were found between men and women.

The DF-group scored significantly higher on the inherent Temperament subscale Harm Avoidance (fatigability and asthenia, HA) compared to a control group. They can be described as astenic, with less energy than most people. The high score in Harm Avoidance may constitute a common tendency to both depression and anxiety disorders (72, 126-128). They recover from minor illnesses or stress more slowly than others do. The presences of depression, anxiety, stress and physical symptoms supports the view that the DF patients should be labelled as having a somatic syndrome (72) since they experience and communicate mental distress as physical symptom. Furthermore, the DF group scored close to significantly higher on the psychosocially learned Character subscale Self-Directedness (self-acceptance, SD) compared to a control group. Which describes them as being self-confident and able to recognize and accept both their strengths and limitations (125). The findings with high Self-Directedness (SD) indicate that the DF patients may be self-confident and have an unrealistic view of their limitations and capacity, which in combination with high Harm Avoidance (fatigue and asthenia, HA) may result in an increased psychosocial vulnerability (table 5).

Table 5. Multiple comparisons of the TCI temperament and character dimensions and subscales of patients with DF (n=26) and EMF sensitivity (n=33) and of the control group (n=67).

TCI dimensions and subscales	DF group (a)	EMF group (b)	Control group (c)	<i>F</i>	<i>P</i>	
	Mean ± SD	Mean ± SD	Mean ± SD			
Persistence (P)	4.2±1.9	4.6±1.8	3.7±1.7	3.37	0.038	b>c
Fatigability and asthenia (HA4)	4.9±2.2	3.8±2.7	2.7±1.8	9.75	<0.001	a>c
Self-acceptance (SD4)	9.3±2.1	8.7±2.2	8.0±2.4	3.19	0.052	a>c

Significant differences between the groups are presented. The Bonferroni test for corrections of multiple comparisons was used.

Women in the DF-group scored higher than men on the Temperament subscales Novelty Seeking (NS) and Reward Dependence (RD), they can be described as being more impulsive and disordered. Somatic anxiety has been found to correlate with Novelty Seeking (NS) and refer to diverse bodily sensations, such as aches, pain and frequent autonomic disturbances (129). For women in the DF group, the combination of high Reward Dependence (RD) and Novelty Seeking (NS) may produce a vulnerable personality that is manifested in over-involvement with other people, loss of objectivity (Reward Dependence, RD), impulsiveness and disorder (Novelty Seeking, NS), which can result in increased somatic anxiety. The experience of this somatic anxiety might be attributed to the toxic effects of dental fillings.

Regarding gender differences, women in the DF-group and also in the control groups scored higher than men on the Temperament subscale Reward Dependence (RD), indicating that women are more tender-hearted, warm, dependent, sensitive and sociable than men. Also Brändström et al. (130) found differences between women and men, including the Reward Dependence (RD), and they suggested that these differences might not only reflect genetically determined influences but also occur with rearing influences directed toward female and male behavioral stereotypes and the interaction of these factors during the life span.

In the present study no significant differences were found between the EMF- or the DF-patients on the TCI dimensions and subscales, which indicates that these groups are quite similar regarding personality. However, compared to the control group, these results indicate that an inherent personality factor may be important in the development of symptoms in the EMF-group, while both inherent and psychosocially learned personality factors may be important in the DF-group (125).

Self-image

When measuring self-image, all patients with oral lesions were excluded, since oral lesions may explain the perceived symptoms. The patients were then divided into subgroups according to symptoms, one group of patients with local symptoms only (LSO), and the other group with Multi-Symptoms (M-S), i.e. both local and general symptoms. As a measure of self-image, the introvert version of Structural Analysis of Social Behavior (SASB) (87, 88) was used. The mean ratings of the positive clusters were used as a measure of a positive self-image, and the mean of the negative clusters as a measure of a negative self-image, also the spontaneous and controlled clusters were used (figure 5).

Both the LSO-group and the M-S-group scored significantly higher on “spontaneous” and “positive self-image” than the reference group (Table 6). On the cluster “controlled” both groups scored lower than the references and on the cluster “negative self-image” both groups scored higher than the references, but neither of the differences was significant (Table 6).

Table 6. SASB scores of the two the subgroups LSO and M-S and the the reference group. Mean score, standard deviation and p-values are shown.

Parameters SASB	Local symptoms only (a)			Multi- symptoms (b)			Reference group (ref)			p-value
	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Spontaneous	52	60.6	31.8	181	57.4	30.2	135	42.5	15.2	a>ref 0.00 ★ b>ref 0.00 ★
Controlled	49	44.7	33.5	179	46.8	34.4	135	50.7	18.1	a<ref 0.65 b<ref 0.70
Positive	53	72.3	20.4	181	72.0	27.4	135	56.5	15.4	a>ref 0.00 ★ b>ref 0.00 ★
Negative	50	22.4	18.1	181	23.8	22.0	135	21.3	16.4	a>ref 1.00 b>ref 0.82

★ p <0.05

As both groups rated significantly higher on the “spontaneous” and “positive self-image” clusters, the patients can be described as being impulsive (having a higher level of spontaneity) and thus in combination with a pronounced positive self-image can result in difficulties in setting limits. However, difficulties in setting limits in combination with high demands may result in mental stress. The stress-related symptoms can be manifested as fatigue and

concentration difficulties or increase the sensitivity to environmental factors, such as dental materials

Self-Image has also been studied in other patient groups with environmental intolerance such as sensitivity to electromagnetic fields and symptoms attributed to Indoor Environment. Bergdahl et al. (6) measured self-image in patients with sensitivity to electromagnetic fields and they found that the patients scored higher on the “spontaneous” and “positive self-image” cluster and normal on the “negative self-image” on the SASB. They suggested that individuals with this self-image might have an unrealistic view of their own capacity, which can result in an increased psychosocial vulnerability and in turn result in stress-related symptoms (6). Also Edvardsson et al. (4) found that female patients with symptoms attributed to Indoor Environment rated higher on the “spontaneous” and “positive self-image” cluster and lower on the “controlled” and “negative self-image” cluster compared to controls. This combination was interpreted as contributing to the risk of developing long-standing symptoms under certain circumstances.

These three patient groups with symptoms attributed to environmental intolerance: dental materials, electromagnetic fields or indoor environment, rated significantly higher on the “spontaneous” and “positive self-image” cluster on the SASB compared to their controls. Thus, the result can be interpreted as these three patient groups are similar concerning self-image and have a higher level of mental stress, which in turn can increase the sensitivity to environmental factors.

Psychological symptoms

To assess psychological symptoms, The Symptom Check List 90 (SCL -90) was administrated (91, 92). The somatization, depression and anxiety was measured and to measure the level of psychological symptoms The Global Severity Index (GSI) was used, i.e. the mean of all 90 items, as it is the best single indicator of severity of disorder according to Derogatis (131).

In groups of patients with symptoms, Local Symptom Only (LSO) and Multi-Symptoms (M-S), the SCL-90 showed that the Multi-Symptoms (M-S) group scored significantly higher than the reference group on the term “somatization” and also significantly higher than the group with Local Symptom Only (LSO). Furthermore, the M-S-group scored significantly higher on the term “depression”, on “anxiety” and also on the GSI scale compared to the reference group. The LSO-group did not differ on any of these subscales (table 7).

In the groups of patients with lichenoid contact reactions (LCR) and oral lichen planus (OLP), no significant differences were found on the GSI scale neither between the two groups of patients, LCR or OLP, nor compared to the references (table 7).

Table 7. SCL-90 scores of the subgroups LSO, M-S, LCR, OLP and the reference group.

Parameters SCL-90	LSO (a)			M-S (b)			Reference (ref)			LCR (c)			OLP (d)			p-value
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Somatization	57	0.8	0.7	187	1.2	0.8	69	0.6	0.6	31	0.7	0.6	13	0.8	0.8	a>ref 0.35 b>ref 0.00★ b>a 0.00★ c>ref 1.0 d>ref 0.48 c<d 1.0
Depression	56	0.7	0.6	187	0.8	0.7	69	0.5	0.5	31	0.6	0.7	13	0.4	0.6	a>ref 0.14 b>ref 0.00★ b>a 0.93 c>ref 1.0 d<ref 1.0 c>d 1.0
Anxiety	56	0.4	0.5	187	0.6	0.6	69	0.4	0.4	31	0.3	0.4	13	0.2	0.4	a=ref 1.0 b>ref 0.02★ b>a 0.32 c<ref 0.91 d<ref 1.0 c>d 1.0
GSI	58	0.5	0.5	187	0.6	0.5	69	0.4	0.4	31	0.4	0.4	13	0.3	0.3	a>ref 0.34 b>ref 0.00★ b>a 0.46 c=ref 1.0 d<ref 1.0 c>d 1.0

★ p < 0,05

The GSI-scale is a symptom index and includes somatization. The results in present study results can be interpreted as there were clear tendencies toward somatization in the M-S-group, which in turn can be considered as reflecting either secondary manifestations because of illness, or an unmanageable social situation. Also Langworth et al. (25) found a clear tendency to somatization in patients with illness attributed to dental fillings. Their results are in accordance with the result of Bratel et al (49), who found that stress-related somatoform disorders were more common in patients with symptoms related to amalgam fillings than in a control group. On the other hand, compared to the reference group the patients in the LSO-, LCR- and OLP-groups did not differ significantly on the GSI-scale which may be interpreted as that they had no tendency to somatization (table 7).

Concerning psychological symptoms in the present study, patients with LSO, M-S, LCR and OLP are unequal. The M-S-group had a significantly higher GSI-value, which indicates that they are more psychologically stressed than the other patient groups (LSO, LCR, and OLP) and also compared to the reference group.

Stress

In the group of patients with oral lichen, stress during the past month was measured by using the General Perceived Stress Questionnaire (PSQ) (93, 94). The results of the General Perceived Stress Questionnaire showed that there were no significant differences neither between the two groups of patients, LCR or OLP, nor compared to the references ($p = 0.643$) (table 8).

Table 8. Score for The General Perceived Stress Questionnaire (PSQ) in the patients with LCR and OLP compared to a reference group.

Parameters	Lichenoid contact reaction (LCR) (a)			Oral lichen planus (OLP) (b)			Reference group (ref)			p-value
	N	Mean	SD	N	Mean	SD	N	Mean	SD	
PSQ	31	0.23	0.14	13	0.18	0.11	418	0.21	0.13	a>ref 1.0 b<ref 1.0

★ $p < 0,05$

Stress occurs when environmental demands overwhelm the individual resources and threaten the persons' well-being (132). To measure stress, PSQ was developed (93), and is one of the most used instruments to measure stress process in psychosomatic research. It has also been associated with somatic complaints and has a good predictive value in stress-related diseases (133, 134). Therefore the PSQ was chosen to measure stress in the patients with oral lichen. The results in the present study are not in agreement with results in other studies, for example Lundqvist et al. (59) who found that depression, anxiety and stress are more common in patients with erosive lichen planus. Furthermore, Koray et al. (135) found that anxiety was more frequent in patients with OLP.

It is known that severe symptoms can be stressful but neither the patients

with LCR nor the patients with OLP experienced more stress compared to the reference group. An explanation could be that the patients in the present study had no erosive oral lichen planus or severe symptoms. They were referred for an examination of oral signs attributed to their dental materials. Patient with erosive oral lichen or severe symptoms probably would have been referred directly to an oral surgeon at the Oral and Maxillofacial Surgery, School of Dentistry, Umeå, or to the Department of Public Health and Clinical Medicine/Dermatology and Venereology, Umeå.

Methodological issues

The patients in the present studies does not represent a randomized sample of the population, but should rather be considered a stratified sample. All patients were referred to the Department of Oral Diagnostics, Faculty of Odontology, Umeå University and all patients that fulfilled the inclusion criteria were asked to participate. The stratified sampling raises issues regarding how representative the results are. It can therefore be discussed if the study population represents the general population and to which extent this affects the validity of the results of this study. In turn to increase the external validity of our results an adult Swedish control population was used to determine whether our patients had more and other symptoms than the general population. However, the study population may be representative for patient with the current problems.

Furthermore, a retrospective data collection had to be done for the baseline information because the patients were referred for routine treatment and therefore not recorded for a research purposes. Due to this fact, the data in the dental records were incomplete in some cases and therefore the patients were excluded from the study. However, the examination at baseline was performed using structured interviews written in the dental records. Both at baseline and follow-up the questionnaire was identical. The questionnaire consisted of predetermined questions based on a questionnaire previously used in a research project regarding exposure to sick-buildings and

electromagnetic fields (2, 3, 5, 6), which allowed a comparison and in turn increased the external validity. In spite of the fact that the questionnaires at baseline and follow-up were identical, there is after all a time difference of 2-9 years between the baseline and follow-up. This means that the patients have become older and also that they may have got more symptoms. However, this is inevitable in a study where changes are recorded over time. Also, the questionnaires were answered in different settings, at baseline in the clinic and at follow-up at home. This could have introduced bias to the results since the environment at home is likely to be less stressful compared to the environment at the clinic, which could have affected the answers.

Based on reported symptoms at baseline, the patients were divided into subgroups and some patients may have been misclassified or the patients might have moved between the subgroups since the pattern of the patients' symptoms might have changed over time. Moreover, a minor variation in diagnostic routines due to replacement of the staff at "Utredningsenheten" could have influenced the results of the clinical examination since the baseline examination was collected under a period of eight years.

A methodological problem is the relatively low response rate to the questionnaires (61%, personal letters included). Therefore, every sixth patient was contacted for a telephone interview and a total of 46 patients were interviewed and the most common reason for not responding was dissatisfaction with the questionnaire, especially with the psychological questions. Since it was shown that there were no significant differences between the responders and non-responders, the results seem to be valid for the whole group. Telephone interviews is a valuable instrument, not only to increase the share of responders, but also to produce less biased responses than mail-only protocols (136).

Concerning the clinical examination of oral lichenoid lesions, the response rate was 60%, but the relatively large share of non-responders (40%), was compensated for by a drop-out analysis in which every second drop-out were

interviewed by telephone. The most common reason for not attending the study was the lack of interest to control their lichenoid reactions. The group of dropouts was not significantly different from the study group regarding the parameters recorded in the questionnaire.

The main weakness of our study is that it is not randomized prospective. It is a follow-up of patients referred for symptoms or signs attributed to dental materials and an evaluation of changes in health after replacement of dental materials. It was not possible to randomize the treatment, since many patients exchanged restorations without any recommendation by the researchers to do so but also the opposite happened – patients who were recommended to exchange their restorations did not exchange any restorations. Randomization was not possible.

General conclusion

Symptoms attributed to dental restorative materials has been suggested to be caused by interacting factors of both somatic and mental origin which can explain why the patients were referred to a dental specialist and some of the patients to psychiatric specialist.

Patients with complex symptoms had a more unfavorable long-term prognosis concerning remaining symptoms than patients with local symptoms only. Unchanged complaints were higher among men with complex symptoms than in women. General symptoms had increased while oral symptoms had decreased. Contradictory is that the majority of general symptoms had increased, while the patients perceived that their health had improved. Even if the patients after replacement of their dental restorative materials claimed that the alleviation of their symptoms was an effect of decreased exposure to the materials suspected, there might be other explanations for the patients' improved health. For example, patients' expectations, spontaneous recovery, changes of attitudes and changes in psychosocial situation.

Concerning oral lesions, the lichenoid lesions regressed significantly more often in the group of patients with LCR than in the group with OLP. The remissions of the lesions in the LCR group were more frequent among the patients with total replacement of dental materials compared with those with a partial replacement or no replacement at all. The present study shows that the remission of lesions was greatest among LCR-patients with positive dental screening patch tests in combination with a total replacement of dental materials. Despite an exchange of all restorations among the OLP-patients with a positive patch test, no regression could be seen. In the OLP group the mucosal lesions were probably not caused by contact reactions to their dental materials.

Regarding the personality and the high persistence demonstrated in the Electromagnetic Fields group and the high self-acceptance in the Dental Fillings group seems to represent personalities that could be vulnerable in the demanding society. Anxiety and mental distress could be expressed as various mental and somatic symptoms attributed to dental materials or Electromagnetic fields. Furthermore, the patients with LSO and M-S were significantly more spontaneous and had a more positive self-image than the references. They can be described as being impulsive and in combination with a pronounced positive self-image this may result in difficulties in setting limits. This in combination with high demands may also result in mental stress, which in turn can increase the sensitivity to environmental factors. The patients with LSO, M-S, LCR and OLP differed regarding psychological symptoms. The M-S group had a significantly higher value of GI, which indicates that they are more psychologically stressed than the other patient groups and the reference group. The GSI-scale is a symptom index and includes somatization, indicating that there were clear tendencies toward somatization in the M-S group. Stress was measured in patients with oral lichen and there were no significant differences neither between the two groups of patients, LCR or OLP, nor compared to the reference groups concerning stress.

In the present study, the majority of patients had carried out a partial or a total replacement of their dental restorative materials that was believed to cause their symptoms, and it was more common among patients with multi-symptoms to replace their dental materials than in patients with local symptoms. It was also more frequent among the multi-symptoms group to report that they felt better or had no symptoms after replacement of dental material. The treatment with replacing dental materials gave reported improvement in health and this might be due to several physical symptoms, the high tendency to somatization, and at the same time the treatment of psychophysiological character, exchange of dental restorations, that might explain the experience of improvement in health.

To avoid conflicting encounters with patients presenting symptoms attributed to dental materials it is important for caregivers to listen to the patient's explanatory models and experience of illness, even if a medical answer cannot be given. It is also important that an examination can be made early in the process to be able to explain facts about the suspected material and possible consequences of a removal before the patients have built up a fixed opinion regarding the causes of their symptoms. Information at early stages might be helpful to prevent the patient from searching for explanations from unreliable sources.

In conclusion, symptoms attributed to dental restorative materials seem to have a multi-factorial origin where dental, medical and psychological factors may be involved. If no biomedical answer can be found after the medical and odontological examinations it seems reasonable to consider all aspects of illness, also the psychological aspect, so these patients may also be psychologically investigated, and treated if needed.

Future studies

Since our interdisciplinary research group has been working with different environmentally attributed health problems, except dental materials also

inadequate air quality and sensitivity to electromagnetic fields, a comparison of these patient groups would be of interest in the future. Furthermore, there is a need for a deeper understanding of the patients' experience of living with environmental intolerance, and also to gain insight into the encounters with health care professionals to avoid harmful consultations. To explore such phenomena that are poorly understood, a qualitative method is well suited and could be of help for medical and odontological assessment, and also for treatment planning for these patients. Thus, to gain a deeper understanding of patients with environmental intolerance, a qualitative interview study could be carried out.

The number of dental materials will surely increase in the future and the content will surely be more complex – the particles might decrease in size and this might alter the health effects of the compounds. Therefore, it is important to evaluate possible reactions to new and rather complex materials. Since no clinical studies are large enough to detect unusual reactions a mandatory and functioning reporting system for adverse effects might be a useful method to detect unusual reactions.

However, despite that the use of mercury and therefore also dental amalgam is prohibited since 2009, the discussion regarding health effects of dental materials will continue. Today hot topics are the possibility of an adverse effect of high fluoride exposure on children's neurodevelopment (137) and also dental materials containing bisphenol A (138) and its' possible effects of general health. Another problem might be that the sizes of the particles in our dental materials are decreasing and this might give new and unexpected health effects. Thus, the dental materials suspected to cause adverse health effects will change over time.

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