

Mercury sensitisation: review, relevance and a clinical report

V. K. Bains,¹ K. Loomba,² A. Loomba³ and R. Bains⁴

IN BRIEF

- Aids understanding of the safety and reliability of amalgam usage.
- Mercury sensitisation and mercury pollution from dentistry are insignificant compared to that from industrial use and natural sources.
- No valid scientific studies have ever shown that dental amalgam poses a health hazard; evidence supports the safety of amalgam restorations.

Eczematous eruptions may be produced through topical contact with mercury and by systemic absorption in mercury sensitive individuals. Mercury is considered a weak sensitiser and contact with mercury salts such as chloride or ammonium chloride may cause hypersensitivity leading to contact dermatitis or Coomb's Type IV hypersensitivity reactions. The typical manifestation is an urticarial or erythematous rash, and pruritis on the face and flexural aspects of limbs, followed by progression to dermatitis. True allergy to mercury is rare but is more common in females. Exposure to mercury vapour produced in operating rooms is the main concern for dentists. **Every effort should be made to avoid contact with mercury vapour if possible by using barrier techniques, reducing the temperature of the operating room and of the amalgam restoration. Air conditioning and proper ventilation of the operating room, the use of coolant sprays, good suction and proper handling of amalgam waste is recommended.** Various reports show the use of MELISA® (memory lymphocyte immunostimulation assay) and patch tests in determining mercury sensitivity. Topical application of glucocorticoids and dimethisone is helpful.

INTRODUCTION

The twentieth century saw great interest in the use of dental amalgam including the very well known 'amalgam war'. Amalgam related issues were debated and explored at length. The term 'Amalgam is Standard' used by Dr Miles Markley was tested extensively.¹ However, according to Djerassi *et al.*,² B. M. Eley³ and Duxbury *et al.*⁴ adverse tissue reactions are infrequent. The dental devices panel of the FDA, during its review on 20 March 1991, concluded 'that none of the data presented show a direct hazard to humans from dental amalgams'.⁵ According to J. E. Dodes⁶ the evidence supporting the safety of amalgam restorations is compelling as data strongly suggest that mercury levels many times

higher than those associated with a mouth full of amalgam pose no risk of adverse health effects. Nonetheless, allergic reactions to silver amalgam are known to occur and often the importance of a proper history and related sensitisation are not elicited, thereby leading to misleading conclusions. This emphasises the need to focus more intensely and in depth on such occurrences. An apparent allergic case occurring in our clinic led us to look in more depth at the history and review the literature in an effort to increase our knowledge. This article intends to critically review the literature and to report a case of mercury allergy in a dental student; it will emphasise the rarity of mercury allergy occurring due to dental amalgam usage and highlight the analytical attention it requires, particularly by those countries that are banning/restricting the use of dental amalgam.⁷

REVIEW

The development of an allergic reaction has often been traced to sensitisation to a mercury containing preparation such as a thermometer, dental amalgam, tattoos, mercurochrome, weed killers,

fungicides, industrial germicides, some antiseptic ointments, cosmetic products, pollution or natural sources as deep water fish etc.^{4,8,9} Although contact dermatitis or Coomb's Type IV hypersensitivity reactions represent the most likely allergic side effects to mercury in dental amalgam,^{10,11} mercurial stomatitis represents the earliest allergic observation, reported as early as 1935 by McGeorge^{12,13} and in 1936 by Akers¹⁴ after ingestion of mercury and bismuth for the treatment of syphilis. Eczematous eruptions may be produced by topical contact with mercury and by systemic absorption in mercury sensitive individuals.¹⁵ Oral lichenoid reactions adjacent to amalgam fillings have also been reported to occur.^{4,16,17} Although the incidence of mercury allergy is rare, members of the dental profession are in a high risk group. A study of dental students showed a statistically significant increase in the rate of mercury hypersensitivity from before the students began their studies to the final years of their courses.¹⁸ A preliminary study on two subjects by Eggleston¹⁹ suggested that dental amalgam can adversely affect the quantity of T lymphocytes. Eley *et al.*²⁰ showed

^{1,2}Periodontics, Saraswati Dental College and Hospital, 233, Tiwari Ganj, Faizabad Road, Chinhat, Lucknow, 227105, India; ^{3,4}Chatrapati Shahuji Maharaj Medical University, Lucknow, 226016, India
*Correspondence to: Dr Vivek Bains
Email: doc_vivek76@yahoo.co.in

Refereed Paper

Accepted 23 April 2008

DOI: 10.1038/sj.bdj.2008.843

©British Dental Journal 2008; 205: 373-378

that there is a reduction in the production of IL-2 and TNF- α in a group sensitive to mercury. Various reports show the use of MELISA^{16,21-24} (memory lymphocyte immunostimulation assay) and patch test^{16,17,25-27} in determining mercury sensitivity. Taking a detailed history, careful handling using a barrier technique or completely avoiding exposure to mercury is advocated in mercury sensitive individuals.

Mercury exposure and portal of entry

Humans are exposed to mercury from a variety of sources in addition to dental amalgams.²⁸ Jones⁷ in his opinion article stressed the fact that 50% of environmental mercury pollution comes from natural sources. Industrial uses of mercury today in chloralkali (bleach), electrical equipment, paints, thermometers, dentistry and in laboratories result in about 25%, 20%, 15%, 10%, 3% and 2% respectively of total mercury exposure.²⁹

Mercury occurs in three forms as metal (Hg⁰), inorganic ion (Hg²⁺) or in one of several organic forms such as ethylmercury, methylmercury,^{4,28} phenylmercury, and thimerosal.²⁴ Methyl mercury is the most toxic form of mercury and is also very efficiently absorbed from the gut (90-95%).²⁸ Methyl mercury has no direct significance to dentistry^{28,30} as it is not produced from amalgams but is generally a product of bacteria or other biological systems acting on metallic mercury.^{6,28,30} The high levels of methylmercury in the flesh of aquatic animals such as swordfish, tuna, whales and seals come from natural sources, such as hydrothermal vents or deep ocean sediments – the oxygen-free habitats favoured by the methylating bacteria.^{31,32}

The production of industrial mercury waste (during production of electrolytic chlorine, electrical apparatus and paints) and subsequent contamination of fresh and salt water fish that may be consumed, is another primary source of methyl mercury.^{21,23,24} One such example is the Minamata disaster in Japan in 1956, which resulted from the dumping of mercury compound in Minamata Bay.^{7,33} Acid rain, another product from industrial pollution, also increases the

level of mercury eroded from rocks.²⁷

The absorption of ionic mercury is poor (1-7%).²⁸ In the past systemic mercury was used for syphilis,^{13,14} ammoniated mercury for psoriasis, mercurochrome as an antiseptic, merthiolate as a preservative, mercury oxide in golden eye ointment,¹⁵ calomel (mercurous chloride) and organomercurials injection as diuretics.^{29,34} In many urban areas of the United States, religious supply stores known as 'botanicas' recommend carrying mercury as an amulet in a sealed pouch or pocket or to sprinkle mercury in the home to attract luck, money and love, to protect against evil, or to speed the actions of spiritual works, occult magic and folk medicines, especially in Latin America.^{35,36} Among *hatters*, occupational exposure of fumes from mercury solution, commonly used during the process of turning fur into felt, resulted in 'mad hatter disease'.³⁷ Preservatives in cosmetics (mascara, eyeliner, eye shadow and eye pencils) as phenylmercury;⁸ Thimerosal in vaccines;²⁹ automotive light switches;^{38,39} children's toys with mercury switches and mercury containing batteries;^{39,40} amalgam tattoos;⁴ dental amalgams;^{2,4,15,18,41-44} and broken thermometers⁴¹ are further potential sources of mercury sensitisation.

Metallic mercury gains access to the body via the skin or as a vapour through the lungs. Ingested metallic mercury is poorly absorbed by the gut (0.01%), so the primary portal into the body is through inhalation of mercury vapour.²⁸ Exposure to mercury metal, particularly its vapour, is the significant factor to consider for dentists and patients.⁶ White and Brandt¹⁸ showed that there is an increase in the development of hypersensitivity to mercury as students progress through dental school and also concluded that exposure to mercury during the preparation of silver amalgam definitely presents an additional occupational hazard as an allergen in the dentist. In the dental surgery, vaporisation of mercury results from various mercury spills, and another potential source of mercury is the routine squeezing by hand of mercury from a wet trituration mix and inhalation of amalgam particles during removal of an old restoration. Thus, total mercury

levels in dental personnel is contributed to by the atmosphere, direct contact and systemic sources, and the mercury content of exposed hair and nails is about four to seven times higher than in their non-exposed tissue.⁴⁵ Battistone *et al.*⁴⁶ conferred the mean blood mercury levels for all the dentists to be about 8.2 ng Hg/ml, and for general dental practitioners and specialists separately, the mean values were 8.8 and 6.3 ng Hg/ml. The threshold limit value (TLV) of a substance is the airborne concentration to which nearly all workers can be exposed eight hours a day, five days a week for prolonged periods without suffering adverse health effects which is about 0.05 milligrams Hg per cubic millimetre.^{47,48} Mantya and Wright⁴⁹ advocated that mercury air concentrations in the dental surgery should be controlled so that employees are not exposed to mercury levels greater than 0.05 mg/m.³ Also, Pagnotto and Comproni⁵⁰ and Naleway *et al.*⁵¹ reported that levels of mercury in the urine of dental personnel were usually below the acceptable limit of 0.15 mg/litre; a normal mercury level in urine is 0.02 mg/litre.⁴⁷ Total daily intake of mercury for individuals with no occupational exposure to mercury is estimated to be about 10 to 20 μ g.⁵² In contrast to Vimy and Lorscheider,⁵³ Berglund⁵⁴ estimated that the average daily dose of mercury inhaled from amalgam restorations was 1.7 μ g, which is about 1% of the dose obtained from the WHO threshold limit value (TLV = 50 μ g Hg/m³) for the work environment.

Mercury hypersensitivity

Mercury is considered a weak sensitiser and contact with mercury salts such as chloride or ammonium chloride may cause hypersensitivity leading to contact dermatitis⁵⁵ or Coomb's Type IV hypersensitivity reactions.^{10,56} Such reactions most commonly affect the skin. The typical manifestation is an urticarial or erythematous rash, and pruritis on the face and flexural aspects of limbs, followed by a progression to dermatitis. The lesions may start as early as few hours to one to two days after exposure.^{4,43,44} Usually the lesions last from about 10-14 days^{4,41,44} to 2-3 weeks.⁴³ The patient may develop a rise in temperature

a few hours after sensitisation with mercury as shown in a case report by Spector.⁴⁴ Eversole⁵⁷ and Duxbury *et al.*⁴ described a phenomenon manifested as immediate contact stomatitis (immediate type hypersensitivity),⁵⁸ or in the skin, systemic eczematous contact-type dermatitis. Intraoral mucosal lesions in the form of mucosal swelling, a burning sensation, oozing eczema or an erosion may develop in an area with direct contact with amalgam fillings.⁴

Oral lichen planus⁵⁹ and lichenoid reaction^{17,60,61} represent the oral manifestation of a chronic irritation or contact lesion in mercury sensitive patients. Holmstrup⁶² and Bratel *et al.*⁶³ reported that contact lichenoid lesions develop as either a clinical manifestation of a delayed hypersensitivity or a chronic non-specific toxic reaction. A cell mediated autoimmune response in lichen planus to basal keratinocytes is supported by recent studies which show that mercury in dental amalgam may induce keratinocyte ICAM-1 expression, increased binding of T-cells to normal keratinocytes, and increased production of TNF- *in vitro*.⁶⁴ Bolewska *et al.*⁶⁵ found fine particulate mercury deposits in lysosomes of fibroblasts and macrophages within the contacting lichenoid lesions. Mercury exposure can elicit IgE and IgG formation and glomerular deposition of later in glomerulopathy may contribute to nephrotoxicity of mercury.⁶⁶ Reports suggest that often dental amalgam contributes to diverse illnesses through reduction of immunocompetence by mercury released from amalgam,¹⁹ however, a study by Mackert *et al.*⁵⁶ provide no such indication that the presence of amalgam restorations adversely affect the human immune system nor do they support the assertion that mercury from dental amalgam produces 'reduced immunocompetence'.

Frequency of mercury allergy

True allergy to mercury is rare but is more common in females.^{4,24} A North American contact dermatitis group reported allergy to mercury in only 3% of the subjects in a double blind study, and 20% of these (0.6%) had a skin condition or a history of a skin condition at the time of testing.⁵² In some

reports, less than 2% of patients have been found to react to amalgam in patch testing and 37% of these were found to be allergic to mercury.²⁰ In contrast, Djerassi and Berova² showed that 16% of subjects with amalgam restorations had positive reactions to mercury using 1% mercuric chloride as an epicutaneous patch test agent in a non-double-blind study. Despite this, in patients with lichen planus the frequency of mercury hypersensitivity is between 16% and 62%; in non-selected population samples it has been reported between 3.2% and 4.9%.⁶⁷⁻⁷⁰

Allergy tests

The first step in recognition of allergy induced diseases is a detailed history of the present complaint and the clinical course. Hypersensitivity reactions which are cell mediated such as contact dermatitis are demonstrated by using patch testing.⁵⁵ The method includes the epicutaneous application of a specific allergen at a defined concentration and in a defined vehicle which will induce a cutaneous inflammatory reaction in a sensitised person, but will cause no reaction in a non-sensitised person. Fregrert⁷¹ and many others^{2,15,69} described a standard series of dental materials applied to the skin to carry out the epicutaneous test. Hensten-Apaetersen and Holland composed a standard series of allergens for use in epicutaneous tests to elucidate possible contact allergy to amalgam.⁷¹ Dental series epicutaneous test batteries of patch test (Trolab® allergens⁷²) are also commonly used.⁷³ Namikoshi *et al.*⁷⁴ performed an epicutaneous patch test in 95 participants and found eight of the 17 allergic responders (in which 10.5% were positively tested with mercury) had a history of dermatitis from metal contact. Lssa *et al.*⁷⁵ found the frequency of positive patch tests to mercury compounds in patients with OLLs to be 47% and other reports show a variation between 16 and 68%.⁷⁵⁻⁷⁷ While Thornhill *et al.*⁷⁸ concluded strong associations, in contrast Lssa *et al.*⁷⁵ demonstrated that a patch test is a limited predictor for amalgam replacement. Bratel *et al.*⁶³ argued that a patch test does not provide an adequate diagnostic tool as it is possible that lichen

planus patients can be hypersensitive to mercury despite a negative skin patch test. Also many anti-amalgamists use a patch test with a dilute solution of corrosive mercury salts that cause the skin to redden and possibly swell. The reaction is misinterpreted as a sign of mercury allergy or toxicity^{81,82} and furthermore the National Council Against Health Fraud recommended in 2002 that there is no logical reason to worry about the safety of amalgam fillings.⁸¹

Metal induced hypersensitivity in humans is based upon the reaction of the allergen with the surface of memory T-lymphocytes sensitised to a specific allergen previously. On contact with the allergen, memory cells become activated and begin to produce lymphokines.²³ The Lymphocyte Stimulation Test (LST) is based on this interaction of memory cells with antigen and has been used in immunology diagnostic for delayed-type hypersensitivity for decades.⁵⁸ MELISA® (memory lymphocyte immuno stimulation assay test) is a modified lymphocyte stimulation test, based on evaluation of the proliferation of peripheral blood memory cells. It is used to measure immunological sensitisation induced by metals and to screen such individuals.^{22,24,83} Lymphocyte reactivity to metals was assessed by the uptake of tritiated thymidine and is expressed as stimulation index (SI).^{21-24,83} Using MELISA®, Podzimek *et al.*⁸³ found that the lymphocytes of patients with mercury allergy produce less gamma interferon and more anti-sperm antibodies in supernatants after mercury stimulation of their lymphocytes. Various studies had shown that MELISA® is of diagnostic value in determining sensitivity to mercury and other amalgam associated metals and show correlation with the patch test.¹⁶ Henderson *et al.*²¹ concluded that the presence of mercury-reactive lymphocytes in blood cannot be used as a specific diagnostic test for dental metal associated illness, but rather reflect exposure to mercury.

CASE REPORT

A 23-year-old dental student reported that she had developed rashes on exposed parts of her body after her clinical work during her posting in the



Figs 1 and 2 Red, itchy rash on the neck and arm following contact with mercury while performing amalgam restorations

Department of Operative Dentistry. The rashes developed with itching and redness on the face, neck and flexor surface of the arm within 24-48 hours after coming into contact with mercury while performing amalgam restorations on patients (Figs 1 and 2). The temperature of the affected area was also found to be raised. The eczematous lesions subsided after 7-10 days without medication. Her past history revealed that she was allergic to mercury which she first noticed when she was 18-years-old and had accidentally come into contact with mercury from a broken thermometer. A mild reaction was observed on that occasion. However, her second allergic reaction, which was more pronounced, developed when she initially came into

contact with mercury in dental school during her pre-clinicals. She suffered from swelling and puffiness on the face and neck extending to the axilla. Pruritis and redness of the skin also developed along with increased temperature of the affected region. This, however, subsided itself without any medication. No history of rhinitis or wheezing was reported by the patient after the mercury exposure; however, she was allergic to dust and developed sneezing when exposed to it. There was no history of mercury allergy in her family. Also, there was no history of using any mercury containing medications either locally or systemically. Restoration of any kind was absent in the oral cavity, and no lesions were found in the oral mucosa. To

prevent eczematous lesions her physician advised her to apply Dermashield® (activated dimethisone) on the exposed area before starting work and asked her to apply Clonate® Lotion (0.05% clobetasol propionate) on the lesions.

DISCUSSION

Among the variety of sources of mercury sensitisation, mercury pollution from dentistry is insignificant compared to that from industrial use and natural sources.⁷ Sterzal *et al.*²³ and White and Smith¹⁵ quoted that females have a higher rate of mercury sensitisation than males. This case illustrates that allergy to mercury can occur as a constituent of dental amalgam especially and specifically in subjects sensitised earlier due to a previous cause. Mercury sensitisation developed in the patient when she was exposed accidentally to mercury from a broken thermometer. Duxbury *et al.*⁴¹ reported a similar case. Dental students as they start doing their clinical posting often develop dermatitis if they are allergic to mercury, as reported in this case. This is similar to the study done by White and Brandt¹⁸ who showed that there is an increase in the development of hypersensitivity to mercury from first to final years at dental school. Skin lesions were found in this case similar to those reported by Duxbury *et al.*⁴ and Spector⁴⁴ which develop in about 24-48 hours after mercury exposure and subside after 7-10 days. This shows a delayed hypersensitivity response to mercury similar to those shown by Marshall *et al.*¹⁰ and Markert *et al.*⁵⁶ However, Stejskal and Stejskal⁵⁸ and Podzimek *et al.*⁸³ commented that though most metal hypersensitivity reactions are of Type IV (delayed hypersensitivity), immediate type reactions are also sometimes observed. A second bout of allergic reaction, however, was more pronounced. This therefore represents that a typical hypersensitivity reaction can develop more quickly and with pronounced effects, due to already present sensitised and activated memory cells, as shown by Ferstrom *et al.*⁴³ However, with proper care and prevention the intensity of development of the lesion markedly reduced, as happened in the present case after usage of activated dimethasone and clobetasol propionate lotion.

Laine *et al.*,¹⁷ Eversole and Ringer,⁵⁹ Henriksson *et al.*,⁶⁰ Bahmer⁶¹ and Holmstrup⁶² commented on lichenoid lesions associated with mercury released from dental amalgam restorations. However, no such lesions were found in her oral cavity. This may be attributed to the absence of any restorations in the oral cavity. This again affirms the safety profile of appropriate and judicious usage of silver amalgam even in a sensitised case.

Treatment, care and prevention

A detailed history of occupation, lifestyle, environment etc and further prevention of exposure to mercury is important. Various barrier techniques like using a mask, gloves, hair caps and eye-shields are advised while working. Careful handling of silver amalgam waste should be encouraged as well. As advocated by Dodes,⁶ Mantyla and Wright⁴⁹ and Eley,⁸⁴ the greatest hazard to the dentist and patients is from exposure to mercury metal, particularly its vapour, so it is beneficial to reduce mercury vapour production as much as possible. Mantyla and Wright⁴⁹ further confirmed that mercury volatility increases as the environmental temperature increases. Also trituration, condensing, burnishing and polishing silver amalgam, cutting hardened amalgam, use of ultrasonics on amalgam restorations, mercury spillage, uncovered amalgam scrap and cleaning the floor and the operating room etc are various sources of Hg-vapour production in dental surgeries or departments.^{46,47,49,50,85} Air conditioners and proper ventilation of the operating room, intermittent use of the rotary along with coolant to avoid excess heat, high vacuum suction, proper cleaning and proper handling of amalgam scraps in a covered container or under sulphide solution is advocated to avoid vapour production.^{30,46-50,73} The Council on Dental Materials and Devices advised in 1976 using conventional (manual and mechanical) dental amalgam procedures but not ultrasonic amalgam condensers.⁸⁶ If any sensitised patient requires restorations, materials other than silver amalgam could be considered.⁸⁷

Dermashield (dimethisone) is a silicone polymer. Pharmacologically inert, it

has water repellent and surface tension reducing properties. It is applied to the skin, adheres to it and protects it;³⁴ it can be used to avoid contact with mercury vapour on the skin. This helps in reducing the lesion's development or its intensity. Clonate lotion contains 0.05% clobetasol propionate which is a glucocorticoid used topically for a large variety of dermatological conditions due to their anti-inflammatory, immunosuppressive, vasoconstrictor and antiproliferative (for scaling lesions) property.³⁴ Antihistamines, though used to reduce allergic effects by many,⁴ are not of much use.

CONCLUSION

Allergy to mercury in amalgam is rare, with females being more susceptible. Less than 2% of patients have been found to react to amalgam in patch testing and 37% of these were found to be allergic to mercury; such individuals can be screened using patch and MELISA® tests. Exposure to mercury vapour produced in dental operating rooms is the main concern for dentists – which is very rare with proper handling. Every effort should be made to avoid contact with mercury vapour if possible. The use of barrier techniques is recommended; if exposed, topical application of glucocorticoids and dimethisone is helpful. Thus, with judicious and meticulous usage of amalgam in dentistry it can still prove to be a safe restorative material.

1. Markely M. In Newman S M. Amalgam alternatives: what can complete? *J Am Dent Assoc* 1997; **122**: 66-71.
2. Djerassi E, Berova N. The possibilities of allergic reactions from silver amalgam restorations. *Int Dent J* 1969; **19**: 481-488.
3. Eley B M. The future of dental amalgam implanted in soft tissues – an experimental study. *J Dent Res* 1979; **58**: 1146-1152.
4. Duxbury A J, Watts D C, Ead R D. Allergy to dental amalgam. *Br Dent J* 1982; **152**: 344.
5. Mandel I R. Amalgam hazards. An assessment of research. *J Am Dent Assoc* 1991; **122**: 62-65.
6. Dodes J E. The amalgam controversy. An evidence-based analysis. *J Am Dent Assoc* 2001; **132**: 348-356.
7. Jones D W. A Scandinavian tragedy. *Br Dent J* 2008; **204**: 233-234.
8. Gamiz-Gracia L, Luque de Castro M D. Determination of mercury in cosmetics by flow injection-cold vapour generation-atomic fluorescence spectrometry with on-line preconcentration. *J Anal At Spectrom* 1999; **14**: 1615-1617.
9. Thomson J, Russell J A. Dermatitis due to mercury following amalgam dental restoration. *Br J Dermatol* 1970; **82**: 292-297.
10. Marshall S J, Marshall G W, Anusavice K J. Dental amalgam. In: *Phillips' sciences of dental materials by Anusavice*, 11th ed. p 526. Saunders, 2003.

11. Adams R M. *Occupational contact dermatitis*. p162. Philadelphia: J. B. Lippincott, 1969.
12. Engelman M A, Falls W. Mercury allergy resulting from amalgam restorations. *J Am Dent Assoc* 1963; **66**: 122.
13. McGeorge J R. Mercurial stomatitis. *J Am Dent Assoc* 1935; **22**: 60.
14. Akers L H. Ulcerative stomatitis following the therapeutic use of mercury and bismuth. *J Am Dent Assoc* 1936; **23**: 781.
15. White I R, Smith B G N. Dental amalgam dermatitis. *Br Dent J* 1984; **156**: 259.
16. Stejskal V D M, Forsbeck M, Cederbrant K E, Asteeman O. Mercury-specified lymphocytes: an indication of mercury allergy in man. *J Clin Immunol* 1996; **16**: 31-40.
17. Laine J, Kalimo K, Forssell H, Happonen R P. Resolution of lichenoid lesion after replacement of amalgam restoration in patients allergic to mercury compounds. *Br J Dermatol* 1982; **126**: 10-15.
18. White R R, Brandt R L. Development of mercury hypersensitivity among dental students. *J Am Dent Assoc* 1976; **92**: 1204-1207.
19. Eggleston D W. Effect of dental amalgam and nickel alloys on T-lymphocytes: preliminary report. *J Prosthet Dent* 1984; **51**: 617-623.
20. Eley B M. The future of dental amalgam: a review of the literature. Part 6: possible harmful effects of mercury from dental amalgam. *Br Dent J* 1997; **182**: 455-459.
21. Henderson D C, Clifford R, Young D M. Mercury-reactive lymphocytes in peripheral blood are not a marker for dental amalgam associated disease. *J Dent* 2001; **29**: 469-474.
22. Stejskal V. MELISA – an *in vitro* tool for the study of metal allergy. *Toxicol In Vitro* 1994; **8**: 991-1000.
23. Sterzal I, Prochazkova J, Hrdá P, Bartova J *et al.* Mercury and nickel allergy: risk factors in fatigue and autoimmunity. *Neuro Endocrinol Lett* 1999; **20**: 221-228.
24. Stejskal V D M, Danersund A, Lindvall A, Hudecek R *et al.* Metal-specific lymphocytes: biomarkers of sensitivity in man. *Neuro Endocrinol Lett* 1999; **20**: 289-298.
25. Ostman P O, Anneroth G, Skoglund A. Amalgam assisted oral lichenoid reactions. Clinical and histologic changes after removal of amalgam fillings. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996; **81**: 459-465.
26. Handley J, Todd D, Borrows D. Mercury allergy in a contact dermatitis clinic in Northern Ireland. *Contact Dermatitis* 1993; **2**: 258-261.
27. Burrows D. Hypersensitivity to mercury, nickel and chromium in relation to dental materials. *Int Dent J* 1986; **36**: 30-34.
28. Wataha J C. Biocompatibility of dental materials. In: *Phillips' sciences of dental materials by Anusavice*, 11th ed. pp 171-202. Saunders, 2003.
29. Klaassen C D. Heavy metals and heavy-metal antagonists. In Brunton L L, Lazo J S, Parker K L. *Goodman & Gilman's the pharmacology basis of therapeutics*, 11th ed. pp 1758-1763. McGraw-Hill, 2006.
30. Rupp N W, Paffenbarger G C. Significance to health of mercury used in dental practice: a review. *J Am Dent Assoc* 1971; **82**: 1401-1407.
31. Kraepiel A M L, Keller K, Chin H B, Malcolm E G, Morel F M. Sources and variations of mercury in tuna. *Environ Sci Technol* 2003; **37**: 5551-5558. http://www.cbc.ca/health/story/2003/12/04/mercury_tuna031204.html
32. Smith W E, Smith A M. *Minamata: a warning to the world*. London: Chatto & Windus, 1975.
33. Tripathi K D. Essentials of medical pharmacology, 5th ed. pp 537, 794, 802. New Delhi: Jaypee Brothers Medical Publishers.
34. United States Environmental Protection Agency. Task Force on Ritualistic Uses of Mercury Report. December 2002.
35. Alison Newby C, Riley D M, Leal-Almeraz T O. Mercury use and exposure among Santeria practitioners: religious versus folk practice in Northern New Jersey, USA. *Ethn Health* 2006; **11**: 287-306.

37. Connealy L E. The Mad Hatter Syndrome: mercury and biological toxicity. 2006. www.NaturalNews.com/terms.shtml
38. http://www.glrppr.org/docs/mercury_in_industry.htm
39. <http://www.ci.richland.wa.us/RICHLAND/enviro/docs/51/docs/mercury%20awareness.pdf?CFID=438321&CFTOKEN=76697994>
40. http://www.cleanairfoundation.org/switchout/mercury_canada_so.asp
41. Duxbury A J, Ead R D, McMurrough S, Watts D C. Allergy to mercury in dental amalgam. *Br Dent J* 1982; **152**: 47.
42. Arnold N M. Allergy to mercury in amalgam fillings. *J Am Med Assoc* 1938; **13**: 646.
43. Fernstrom A I B, Frykholm K O, Huldt S. Mercury allergy with eczematous allergy dermatitis due to silver amalgam fillings. *Br Dent J* 1962; **18**: 204-206.
44. Spector L A. Allergic manifestation to mercury. *J Am Dent Assoc* 1951; **42**: 320.
45. Hefferren J J. Usefulness of chemical analysis of head hair for exposure to mercury. *J Am Dent Assoc* 1976; **92**: 1213-1216.
46. Btistone G C, Hefferren J J, Miller R A, Cutright D E. Mercury: its relation to the dentist's health and dental practice characteristics. *J Am Dent Assoc* 1976; **92**: 1182-1188.
47. Eames W B, Gaspar J D, Mohler C M. The mercury enigma in dentistry. *J Am Dent Assoc* 1976; **92**: 1199-1203.
48. Gronka P A, Bobkoskie R L, Tomchick G J, Bach F, Rakow A B. Mercury vapour exposures in dental offices. *J Am Dent Assoc* 1970; **81**: 923-925.
49. Mantyla D G, Wright O D. Mercury toxicity in the dental office: a neglected problem. *J Am Dent Assoc* 1976; **92**: 1189-1194.
50. Pagnotto L D, Comproni E M. The silent hazard: an unusual case of mercury contamination of a dental suite. *J Am Dent Assoc* 1976; **92**: 1195-1198.
51. Naleway C, Sakaguchi R, Mitchell E, Muller T *et al*. Urinary mercury levels in US dentists, 1975-1983: review of health assessment. *J Am Dent Assoc* 1985; **111**: 37-42.
52. Mackert J R. Dental amalgam and mercury. *J Am Dent Assoc* 1991; **8**: 54-61.
53. Vimy M J, Lorscheider F L. Serial measurement of intraoral air mercury: estimation of daily dose from dental amalgam. *J Dent Res* 1985; **64**: 1072-1075.
54. Berglund A. Estimation by a 24-hour study of daily dose of intraoral mercury vapour inhaled after release from dental amalgam. *J Dent Res* 1990; **69**: 1646-1651.
55. Adams S. Allergies in the workplace. *Curr Opin Allergy Clin Immunol* 2006; **19**: 82-86.
56. Mackert J R, Leffell M S, Wagner D A, Powell B J. Lymphocyte levels in subjects with and without amalgam restorations. *J Am Dent Assoc* 1991; **122**: 49-53.
57. Eversole L R. Allergic stomatitides. *J Oral Med* 1979; **34**: 93-102.
58. Stejskal J, Stejskal V D M. The role of metals in autoimmunity and the link to neuroendocrinology. *Neuro Endocrinol Lett* 1999; **20**: 351-364.
59. Eversole L R, Ringer M. The role of dental restorative metals in the pathogenesis of oral lichen planus. *J Oral Surg* 1984; **57**: 383-387.
60. Henriksson E, Mattsson U, Hakansson J. Healing of lichenoid reaction reactions following removal of amalgam. A clinical follow-up. *J Clin Periodontol* 1995; **22**: 287-294.
61. Bahmer K P. Oral lichenoid lesions, mercury hypersensitivity and combined hypersensitivity to mercury and other metals: histologically-proven reproduction of the reaction by patch testing with metal salts. *Contact Dermatitis* 1995; **33**: 323-328.
62. Holmstrups P. Oral mucosa and skin reactions related to amalgam. *Adv Dent Res* 1992; **6**: 120-124.
63. Bratel J, Hakeberg M, Jontell M. Effect of replacement of dental amalgam on oral lichenoid reactions. *J Dent* 1996; **24**: 41-45.
64. Position paper. Oral features of mucocutaneous disorders. *J Periodontol* 2003; **74**: 1545, 1545-1556.
65. Bolewska J, Holmstrup P, Moller-Moadsen B, Kenrad B, Danscher G. Amalgam associated accumulations in normal oral mucosa, oral mucosal lesions of lichen planus and contact lesions associated with amalgam. *J Oral Pathol Med* 1990; **19**: 39-42.
66. Templeton D M. International union of pure and applied chemistry. Mechanisms of immunosensitization to metals (IUPAC Technical report). *Pure Appl Chem* 2004; **76**: 1255-1268.
67. Eversole L M. Allergic stomatitis. *J Oral Med* 1979; **34**: 93-102.
68. Bolewska J, Hnsen H J, Holmstrup P, Pindborg J J, Stangerup M. Oral mucosal lesions related to silver amalgam restorations. *Oral Surg Oral Med Oral Pathol* 1990; **70**: 55-58.
69. Lundstrom I M C. Allergy and corrosion of dental materials in patients with oral lichen planus. *Int J Oral Surg* 1984; **13**: 16-24.
70. Finne K, Goransson K, Winckler L. Oral lichen planus and contact allergy to mercury. *Int J Oral Surg* 1982; **11**: 236-239.
71. In Holmstrup P. Oral mucosa and skin reactions related to amalgam. *Adv Dent Res* 1992; **6**: 120-124.
72. www.hermal.de/her_en/pages
73. Ismail S B, Kumar S K S, Zin R B. Oral lichen planus and lichenoid reactions: etiopathogenesis, diagnosis, management and malignant transformation. *J Oral Sci* 2007; **49**: 89-106.
74. Namikoshi T, Yoshimatsu, Suga K, Fujii H, Yasuda K. The prevalence of sensitivity to constituents of dental alloys. *J Oral Rehabil* 1990; **17**: 377-381.
75. Lssa Y, Duxbury A J, Macfarlane T V, Burtnton P A. Oral lichenoid lesions related to dental restorative materials. *Br Dent J* 2005; **198**: 361-366.
76. Bolewska J, Hansen H J, Holmstrup P, Pindborg J J, Stangerup M. Oral mucosal lesions related to silver amalgam restorations. *Oral Surg Oral Med Oral Pathol* 1990; **70**: 55-58.
77. Laine J, Kalimo K, Happonen R P. Contact allergy to dental restorative materials in patients with oral lichenoid lesions. *Contact Dermatitis* 1997; **36**: 141-146.
78. Thornhill M H, Pemberton M N, Simmons R K, Theaker E D. Amalgam contact hypersensitivity lesions and oral lesion planus. *Oral Surg Oral Med Oral Pathol Endod* 2003; **95**: 291-299.
79. Wong L, Freeman S. Oral Lichenoid Lesions (OLL) and mercury in amalgam fillings. *Contact Dermatitis* 2003; **48**: 74-79.
80. Lind P O, Hurlen B, Lyberg T, Aas E. Amalgam related oral lichenoid reaction. *Scand J Dent Res* 1986; **94**: 448-451.
81. National Council Against Health Fraud. Position Paper on Amalgam Fillings, 2002. www.ncahf.org
82. Fisher A A. The misuse of patch test to determine 'hypersensitivity' to mercury amalgam dental fillings. *Cutis* 1985; **35**: 109, 112, 117.
83. Podzimek S, Prochazkova J, Bultasova L, Bartova J *et al*. Sensitisation to inorganic mercury could be a risk factor for infertility. *Neuro Endocrinol Lett* 2005; **26**: 277-282.
84. Eley B M. The future of dental amalgam: a review of the literature, part 2- mercury exposure in dental practice. *Br Dent J* 1997; **182**: 293-297.
85. Grossman L I, Dannenberg J R. Amount of mercury vapor in air of dental offices and laboratories. *J Dent Res* 1949; **28**: 435-438.
86. Recommendations in mercury hygiene. *J Am Dent Assoc* 1976; **92**: 1217.
87. Newman S M. Amalgam alternatives: what can compete? *J Am Dent Assoc* 1997; **122**: 66-71.