There is a substantial proportion of the population using fixed metallic oral appliances, such as crowns and bridges, which are composed of various dental alloys. These restorations may be associated with a number of effects on oral health with variable degrees of severity, to review potential effects of using fixed metallic oral appliances, fabricated from various alloys. The MEDLINE/PubMed database was searched using certain combinations of keywords related to the topic. The search revealed that burning mouth syndrome, oral pigmentation, hypersensitivity and lichenoid reactions, and genotoxic and cytotoxic effects are the major potential oral health changes associated with fixed prosthodontic appliances. Certain oral disorders are associated with the use of fixed metallic oral appliances. Patch test is the most reliable method that can be applied for identifying metal allergy, and the simultaneous use of different alloys in the mouth is discouraged.

**Keywords:** Burning mouth syndrome, dental alloys, fixed prosthesis, hypersensitivity, oral pigmentation

## INTRODUCTION

A substantial proportion of dental patients worldwide use fixed metallic restorations. In Europe, for instance, Sweden reported the highest use of fixed restorations (45%) followed by Switzerland (34%).[1] Another study reported that 12.4% of Finnish men and 12.1% of women have crowns, whereas 4.8% and 8.0%, respectively, have fixed dental prostheses.[2] Although fixed metallic appliances greatly impact patients’ lives,[3] unfortunately, they also alter and modify oral microbial flora.[4]

Many elements are used to form the various dental metal alloys that are cast and formed to be used as fixed oral appliances.[5] Dental casting alloys are widely used in fixed prosthodontic appliances, and they establish a long-lasting contact with adjacent oral mucosa for periods that may cover the remaining lifespan of the patient.[6] Ni–Cr is probably the most popular alloy used for the fabrication of fixed prosthodontic restorations, owing to its improved mechanical properties and relatively low cost.[7] The use of Ni–Cr was cited as one of the factors associated with better survival rates of resin-bonded bridges.[8] Consequently, Ni–Cr and Co–Cr base metal alloys have replaced the more expensive gold in the construction of fixed metal–ceramic restorations to a great extent.[9]

Unfortunately, these restorations are not without cost as these often extend into the gingival sulcus and come in contact with gingival epithelial cells.[9] The adaptation of dental crowns and bridges to the supporting prepared crowns is less than perfect, always creating a gap that promotes bacterial colonization. Microcracks in the structure of these restorations will also do the same.[10,11] The changes in oral microbial flora due to fixed restorations are well documented in literature; however, their effects may be underestimated in patients with systemic diseases.[12,13] Leaching by-products in the oral cavity of corroded metals of dental alloys can lead to adverse tissue reactions.[13] An immunological response may occur locally, leading to oral discomfort that may be manifested clinically as lichenoid reactions and stomatitis.[14] A systemic reaction may develop, eventually leading to delayed hypersensitivity.[14]
Age-related changes in the oral mucosa may complicate the situation. Moreover, taking into consideration the fact that most fixed prosthodontics patients are in the older age range, a higher incidence of complications is anticipated. The decreasing ability of the tissue to repair with age increases the permeability of oral mucosa to toxic substances and makes it more sensitive to mechanical trauma. Furthermore, prosthetic-retained teeth in elderly are particularly susceptible to caries and a higher chance for prosthesis failure.\(^{[15]}\)

Biologic nature of the oral cavity qualifies it to be an active environment for the corrosion of metallic alloys that have low mechanical and biological properties.\(^{[16]}\) Leakage of ions will cause a wide range of biological interactions. The subsequent soft-tissue response can promote the adhesion of bacteria and lead to toxic or subtoxic effects or allergic responses.\(^{[13]}\) Many studies and research works have already demonstrated these mechanisms. Mechanical trauma due to pressure and friction between appliances and tissues can also lead to local tissue reactions. Further, corrosion may adversely influence the mechanical integrity and biocompatibility, leading to compromised esthetics, physical weakness, and health hazards.\(^{[12]}\)

**Materials and Methods**

A literature search was conducted in MEDLINE/PubMed database using the following keyword combinations: fixed dental prosthesis, fixed partial dentures, cytotoxic effects, oral pigmentation, burning mouth syndrome (BMS), allergy, and lichenoid reactions. Only English literature was included, and as it was not the aim of this review to allude to gingival/periodontal diseases as complications of fixed prostheses, all nonrelevant articles were excluded from the study.

**Results**

The above search revealed that there are four major potential oral health effects of fixed prosthodontic appliances: BMS, oral pigmentation, hypersensitivity and lichenoid reactions, and genotoxic and cytotoxic effects as shown in the following Table 1.

**Burning mouth syndrome**

This is portrayed by the unrelenting burning sensation and pain with undetectable oral mucosa changes.\(^{[35]}\) Patients usually complain of a burning sensation that may affect various oral sites but mainly the labial mucosa and the tongue. Its etiology is poorly understood;\(^{[36]}\) however, it may be classified into a primary variant that is related to underlying neuropathy and a secondary variant that may arise as a result of local precipitating factors such as contact hypersensitivity.\(^{[18]}\) It has been stated that the prevalence of BMS may be difficult to determine precisely because of different clinical entities;\(^{[17]}\) however, prevalence varies with age and gender, as it may reach up to 33\% in postmenopausal women.\(^{[18]}\)

Studies that investigated the association between BMS and fixed dental appliances presented contradictory results. Although Marino *et al.* stated that the findings of the patch test for metals were not significantly associated with BMS, they recommended investigating hypersensitivity when evaluating patients with symptoms of BMS.\(^{[18]}\)

Another study showed the salivary concentration of Ni to be significantly higher in subjects with metal dental appliances, but they concluded that BMS is not correlated with higher metal ion concentration in saliva.\(^{[19]}\) Significantly, another study reported that subjects reporting BMS are more likely to have a contact allergy to gold but not mercury.\(^{[20]}\)

**Hypersensitivity and lichenoid reactions**

Lichenoid oral reactions are indistinguishable histologically or clinically from oral lichen planus. However, a known factor can be identified in case of the former lesions.\(^{[39]}\) In some patients, oral lichenoid reactions appear as a result of chronic irritation or a delayed hypersensitivity reaction.\(^{[59]}\) Although dental amalgam is the most commonly implicated dental material for causing lichenoid reactions,\(^{[40]}\) other materials may also be involved. The material used in dental alloys should be biocompatible, and it should not cause toxic or injurious effects when it comes into contact with living tissue. In other words, biocompatible dental materials do not contain toxic elements, and substances do not leach or diffuse or get absorbed into the circulatory system, causing adverse systemic effects, i.e., teratogenic or carcinogenic.\(^{[9]}\) Cobalt, chrome, nickel, palladium, and mercury are widely used in dentistry, and their allergic effect is documented.\(^{[5]}\)

Nickel is known to cause allergy, and the use of alloys containing nickel in dentistry has been associated with allergic reactions.\(^{[9]}\) Nickel dermatitis has also been reported extensively in literature, but the incidence of nickel allergy is reported to be high,\(^{[41]}\) especially in women.\(^{[42]}\) Intraorally, nickel allergy is manifested as a burning sensation, gingival hyperplasia, and lingual paresthesia.\(^{[21]}\) Patients with nickel allergy are more likely to be allergic to cobalt and chromium.\(^{[22]}\) Although gold is suggested as an alternative to nickel in allergic patients, there were sporadic case reports on the development of orofacial granulomatosis in response to gold dental crowns.\(^{[23]}\) The extent of the allergic reaction has been found to correlate positively with the area of
Exposed gold surfaces inside the oral cavity; the more the quantity in the oral cavity, the more the risk of gold allergy. Populations differ in the prevalence of dental gold use. In Sweden, for instance, more than 25% of the population use dental gold.

Palladium is another metal that is extensively reported to cause oral lichenoid reactions in some palladium-sensitive patients. The frequency of lichenoid reactions was reported to be approximately 13%–15% among patients with palladium sensitivity.

### Table 1: Studies presenting oral health effects of fixed metallic appliances

| Study | Type | Method | Results |
|-------|------|--------|---------|
| Baričević et al. | In vivo, analytic case–control | n=30 with fixed prostodontic appliances for 5 years or more, 25 controls | Evidence of DNA damage in buccal cells adjacent to prostheses |
| Imirzalioglu et al. | In vivo, analytic case–control | n=60 high noble and 20 base metal samples of new and recast alloy | Reuse of cast alloy results in reduced cellular activity of culture cells |
| Faccioni et al. | In vivo, analytic case–control | 55 orthodontic patients and 30 controls | DNA damage in oral mucosal cells with fixed appliances |
| Marino et al. | Cohort | n=124 | Allergy (patch test) is not associated with BMS |
| Baričević et al. | Cross-sectional, analytic, case–control | n=85 with and without fixed oral appliances. | Salivary Ni is higher in subjects with appliances but do not correlate with BMS |
| Koch and Bahmer | Cross-sectional analytic | n=194 with amalgam or Au or Pd restorations | High sensitization to Au and Pd. Subjects with BMS have contact allergy to Au |
| Noble et al. | Review and report of 2 cases | n=2 | Ni allergy manifests as: BMS, gingival hyperplasia and lingual paresthesia |
| Syed et al. | Systematic review | | Ni allergy is also linked to Co, Cr allergy |
| Lazarov et al. | Case report | n=2 | Au is linked to cases of orofacial granulomatosis |
| Ahlgren et al. | Cross-sectional analytic study | n=102 | 74.2% of patients with contact dermatitis to gold had gold fillings |
| Duroso and el-Azhary | Retrospective study | n=910 tested, of them: 106 (12.1%) were sensitized to Pd | Significant association between gold surfaces and allergy |
| Ditrichova et al. | Cross-sectional | n=25 with lichenoid lesions | Pd linked to lichenoid reactions in 13%–15% of cases |
| Tian et al. | Case report | n=1 | Traces of O, C, and Na in gingival pigmentation around Ni-Cr crowns |
| Joska et al. | Cross-sectional in vivo | | Oral pigmentation is related to corrosion of alloys. Also, traces of Au in root with Au crowns |
| Yamada and Sato | Case report | n=1 | Gingival stains around Au crowns contain Ag |
| Garhammer et al. | In vivo, cross-sectional | n=28 | Gingival stains around crowns contain Pd, Cu, Au and Ag |
| Wataha et al. | Laboratory, analytic | Cell cultures of macrophages with/without LPS and added metal ions | Ni was the most to induce the release inf. Mediators and tumor necrosis factor-alpha with or without LPS |
| Qiao et al. | In vivo laboratory study | Cell cultures of fibroblasts to study cytotoxicity and DNA damage | Ions induce RNA and DNA changes and apoptosis |
| Geurtsen | Review | | Mutagenic and genotoxic effect on prokaryotic cells in vitro |
| Westphalen et al. | In vivo lab analysis of buccal cells of orthodontic patients | n=20 | DNA damage in oral mucosal cells after fixed ortho. appliances |

BMS=Burning mouth syndrome, LPS=Lipopolysaccharide
**ORAL PIGMENTATION**

Ever since prices of gold increased since the 1980s, nickel-based alloys were introduced as a replacement for their substructure. The complexity of the oral environment causes alloys to continuously corrode, nickel ion (Ni$^{3+}$) among other ions can leach for a prolonged time.$^{[44]}$

It has been claimed that the development of oral pigmentation is closely related to the occurrence of corrosion of dental alloys. In this case, visible areas of linear pigmentation surrounding the restored tooth become evident.$^{[28]}$ Yamada and Sato reported that gingival stains around the margins of gold crowns contain silver.$^{[29]}$ Further, Garhammer et al.$^{[30]}$ reported that such stains around restorations of different alloys contain palladium, copper, gold, and silver. Joska et al.$^{[23]}$ also reported the detection of copper and silver in the root of a tooth restored with a gold-based alloy dental crown.

It has been claimed that the presence of such restorations correlates with the appearance of soluble compounds in the gingival sulcus. The sulcus forms a protected environment for such compounds, facilitating their transport to adjacent soft tissues. Meanwhile, some of these compounds get deposited, producing the typical tissue pigmentation.$^{[28]}$ The mechanism of tissue pigmentation though needs more explanation and further research is needed in this aspect. In a patient with such tissue pigmentation around the Ni-Cr dental crown, another study used energy-dispersive X-ray analysis and reported the identification of C, O, and Na, but no traces of Ni or Cr could be identified.$^{[27]}$

Regardless of the mechanism behind oral pigmentation around fixed dental appliances, there were no reports on the potentially harmful consequences of these pigmentations, apart from the esthetic complaints of the patients. Recently, Ristic et al. indicated that gingival pigmentation seemed to be linked to the impaired periodontal condition of abutment teeth and they recommended careful preparation of abutment teeth to minimize the chance for the occurrence of gingival pigmentation.$^{[45]}$

**GENOTOXIC AND CYTOXIC EFFECTS**

Ni$^{3+}$, Cr$^{3+}$, and other similar metal ions reported to be released from cast alloys are believed to affect gingival fibroblast behavior, altering its proliferation behavior and modifying its metabolism.$^{[31]}$ These ions are also believed to raise the levels of inflammatory mediators and tumor necrosis factor-alpha.$^{[31]}$ DNA and RNA changes and the appearance of protein synthesis promoting oxidative DNA damage could also be detected following the exposure to these leaching ions from cast dental alloys, indicating obvious cytotoxicity.$^{[32]}$ Apoptosis was also noticed.$^{[32]}$ Many studies confirmed the genotoxic and mutagenic effects in prokaryotic and eukaryotic cells of these ions in vitro;$^{[33]}$ however, there are only a few in vivo studies documenting the damage of DNA of oral mucosal cells as a result of such metal release from fixed orthodontic appliances.$^{[16,34]}$

Leaching ions from fixed prostodontic restorations possess genotoxic effects as reported by Baričević et al.$^{[6]}$ Cobalt-chromium-molybdenum and nickel-chromium dental casting alloys were investigated. Results indicated that leached ions might influence the DNA damage of mucosal cells.$^{[6]}$ Another study indicated that Ni-Cr alloys are more cytotoxic than Co-Cr or Au-Pt alloys.$^{[9]}$ The degree of cytotoxicity has been linked to the frequency of melting and casting processes where degenerative changes in cell morphology have been noticed, leading to the recommendation of some researchers to avoid using dental alloys that contain nickel.$^{[46]}$

All researches that could be found in the literature have reported interactions in relation to well-known widely used dental alloys. Little is known or reported about the interaction of oral tissues with the introduction of low-quality material or alloy.

**CONCLUSION**

It can be concluded that fixed metallic oral appliances have potential effects on oral health. Patients complaining of the above-mentioned disorders should be screened by their general dental practitioners for oral prosthetic appliances. A recommended approach is to use patch test, which is the most reliable method for identifying metal allergy.$^{[5]}$ Using a patch test entails the preparation of an ointment or solution that contains a certain concentration of the assumed allergen and its application on the patient’s skin.$^{[5]}$ For example, if a nickel allergy is suspected, diagnosis can be established by patch test using 5% nickel sulfate in petroleum jelly.$^{[21]}$

The knowledge of allergy and corrosion rates of fabricated alloys is required in dentists to minimize the risk of allergic reactions. A previous history of metal allergy entails performing a patch test for the hypersensitive patient, and caution is needed when planning to use different alloys in the mouth.$^{[5]}$ It may be useful to modify the treatment plan of the patient when any of the above diseases is encountered, following the fabrication of fixed dental appliances utilizing metallic components.
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There are no conflicts of interest.

**REFERENCES**

1. Zitzmann NU, Hagmann E, Weiger R. What is the prevalence of various types of prosthetic dental restorations in Europe? Clin Oral Implants Res 2007;18 Suppl 3:20-30.

2. Näpänkangas R, Haikola B, Oikarinen K, Söderholm AL, Remes-Lyly T, Sipilä K, et al. Prevalence of single crowns and fixed partial dentures in elderly citizens in the Southern and Northern parts of Finland. J Oral Rehabil 2011;38:328-32.

3. Al-Omiri MK, Hammad OA, Lynch E, Lamey PJ, Clifford TJ. Impacts of implant treatment on daily living. Int J Oral Maxillofac Implants 2011;26:877-86.

4. Dar-Odeh N, Shehabi A, Al-Bitar Z, Al-Omari I, Badran S, Al-Omiri M, et al. Oral Candida colonization in patients with fixed orthodontic appliances: The importance of some nutritional and salivary factors. Afr J Microbiol Res 2011;5:2155-9.

5. Zhang X, Wei LC, Wu B, Yu LY, Wang XP, Liu Y, et al. A comparative analysis of metal allergens associated with dental alloy prostheses and the expression of HLA-DR in gingival tissue. Mol Med Rep 2016;13:91-8.

6. Baričević M, Ratkaj M, Mladenić M, Želježić D, Kraljević SP, Lončar B, et al. In vivo assessment of DNA damage induced in oral mucosa cells by fixed and removable metal prosthetic appliances. Clin Oral Investig 2012;16:325-31.

7. Sinha N, Gupta N, Reddy KM, Shastry YM. Versatility of PEEK as a fixed partial denture framework. J Indian Prosthodont Soc 2017;17:80-3.

8. Balasubramaniam GR. Predictability of resin bonded bridges – A systematic review. Br Dent J 2017;222:849-58.

9. Imirzalioglu P, Aladağoglu E, Yılmaz Z, Öncüoğlu B, Yılmaz B, Rosenstiel S, et al. Influence of recasting different types of dental alloys on gingival fibroblast cytotoxicity. J Prosthet Dent 2012;107:24-33.

10. Al-Hassan MI, Abu-Hammad OA, Harrison A. Strains and tensile stress distribution in loaded disc-shaped ceramic specimens. An FEA study. J Oral Rehabil 1998;25:490-5.

11. Al-Hassan MI, Abu-Hammad OA, Harrison A. Stress distribution associated with loaded ceramic onlay restorations with different designs of marginal preparation. An FEA study. J Oral Rehabil 2000;27:294-8.

12. Dar-Odeh NS, Hayajneh WA, Abu-Hammad OA, Hammad HM, Al-Wahadneh AM, Bulos NK, et al. Orofacial findings in chronic granulomatous disease: Report of twelve patients and review of the literature. BMC Res Notes 2010;3:37.

13. Schmalz G, Garhammer P. Biological interactions of dental cast alloys with oral tissues. Dent Mater 2002;18:396-406.

14. Vencilikova Z, Benada O, Bártova J, Joska L, Mrklaš M. Metallic pigmentation of human teeth and gingiva: Morphological and immunological aspects. Dent Mater 2007;26:96-104.

15. Giusti L, Steinborn C, Steinborn M. Use of silver diamine fluoride for the maintenance of dental prostheses in a high caries-risk patient: A medical management approach. J Prostheth Dent 2017. pii: S0022-3931(17)30430-4.

16. Battistutta F, Franceschetti P, Cerpelloni M, Fracasso ME. In vivo study on metal release from fixed orthodontic appliances and DNA damage in oral mucosa cells. Am J Orthod Dentofacial Orthop 2003;124:687-93.

17. Lu C, Zheng Y, Zhong Q. Corrosion of dental alloys in artificial saliva with Streptococcus mutans. PLoS One 2017;12:e0174440.

18. Marino R, Capaccio P, Pignataro L, Spadari F. Burning mouth syndrome: The role of contact hypersensitivity. Oral Dis 2009;15:255-8.

19. Barićević M, Mravak-Stipetić M, Stanimirović A, Blanuša M, Kern J, Lončar B, et al. Salivary concentrations of nickel and chromium in patients with burning mouth syndrome. Acta Dermato-Venereol Croat 2011;19:2-5.

20. Koch P, Bahmer FA. Oral lesions and symptoms related to metals used in dental restorations: A clinical, allergological, and histologic study. J Am Acad Dermatol 1999;41:422-30.

21. Noble J, Ahiy SI, Karaiskos NE, Wiltshire WA. Nickel allergy and orthodontics, a review and report of two cases. Br Dent J 2008;204:297-300.

22. Syed M, Chopra R, Sachdev V. Allergic reactions to dental materials-A systematic review. J Clin Diagn Res 2015;9:ZE04-9.

23. Lazarov A, Kidron D, Tulchinsky Z, Minkov B. Contact orofacial granulomatosis caused by delayed hypersensitivity to gold and mercury. J Am Acad Dermatol 2003;49:1117-20.

24. Ahlgren C, Ahnile I, Björkner B, Bruse M, Liedholm R, Möller H, et al. Contact allergy to gold is correlated to dental gold. Acta Derm Venerol 2002;82:41-4.

25. Durosaro O, el-Azhary RA. A 10-year retrospective study on palladium sensitivity. Dermatitis 2009;20:208-13.

26. Nitirchova D, Kapralova S, Tichy M, Ticha V, Dobesova J, Justova E, et al. Oral lichenoid lesions and allergy to dental materials. Biomed Pap Fac Med Univ Palacky Olomouc Czech Repub 2007;151:333-9.

27. Tian M, Ma S, Niu L, Chen J. Gingival pigmentation by Ni-Cr-based metal ceramic crowns: A clinical report. J Prostheth Dent 2016;115:1-4.

28. Joska L, Vencilikova Z, Poddana M, Benada O. The mechanism of gingival metallic pigmentation formation. Clin Oral Investig 2009;13:1-7.

29. Yamada S, Sato Y. Histopathological study of gingival pigmentation caused by full cast crown. Bull Tokyo Dent Coll 1981;22:51-66.

30. Garhammer P, Schmalz G, Hiller KA, Reitinger T. Metal content of biopsies adjacent to dental cast alloys. Clin Oral Investig 2003;7:92-7.

31. Wataha JC, Ratanasathien S, Hanks CT, Sun Z. In vitro IL-1 beta and TNF-alpha release from THP-1 monocytes in response to metal ions. Dent Mater 1996;12:322-7.

32. Qiao GY, Shen QP, Su JS. Study on cytotoxicity of three kinds of dental ceramic alloys on L929 mouse fibroblasts in vitro. Shanghai Kou Qiang Yi Xue 2010;19:72-6.

33. Geurtsen W. Biocompatibility of dental casting alloys. Crit Rev Oral Biol Med 2002;13:71-84.

34. Westphalen GH, Menezes LM, Prá D, Garcia GG, Schmitt VM, Henriques JA, et al. In vivo determination of genotoxicity induced by metals from orthodontic appliances using micronucleus and comet assays. Genet Mol Res 2008;7:1259-66.

35. Scala A, Checchi L, Montecuccchi M, Marini I, Giamberardino MA. Update on burning mouth syndrome: Overview and patient management. Crit Rev Oral Biol Med 2003;14:275-91.

36. Grushka M, Epstein JB, Gorsky M. Burning mouth syndrome. Am Fam Physician 2002;65:615-20.

37. Coculescu EC, Tovaru S, Coculescu BI. Epidemiological and etiological aspects of burning mouth syndrome. J Med Life 2014;7:305-9.

38. Zakrzewska J, Buchanan JA. Burning mouth syndrome. BMJ Clin Evid 2016; pii: 1301.

39. Minciuolo PL, Paolino G, Vacca M, Gangemi S, Nettis E. Unmet diagnostic needs in contact oral mucosal allergies. Clin Mol Med 2016;11:80-3.

40. Thanyavuthi A, Boonchai W, Kasemsarn P. Amalgam contact allergy and eliciting threshold concentrations. Sci Total Environ 2017;579:111-9.

41. Menné T. Quantitative aspects of nickel dermatitis. Sensitization and eliciting threshold concentrations. Scand J Work Environ Health 1997;23:398-405.
determine referral? A retrospective study of 500 children tested between 1995 and 2004 in one U.K. Centre. Br J Dermatol 2006;154:114‑7.

43. Möller H. Dental gold alloys and contact allergy. Contact Dermatitis 2002;47:63‑6.

44. Yu J, Zhao F, Wen X, Ding Q, Zhang L, Wang G, et al. Apoptosis mechanism of gingival fibroblasts induced by nickel ion contained in dental cast alloys. Biomed Mater Eng 2012;22:151‑7.

45. Ristic L, Dakovic D, Postic S, Lazic Z, Bacevic M, Vucevic D. Clinical characteristics of abutment teeth with gingival discoloration. J Prosthodont 2017. doi: 10.1111/jopr.12612.

46. Čairović A, Maksimović V, Radović K, Djurišić S. The effect of recasting on biological properties of Ni‑Cr dental alloy. Srp Arh Celok Lek 2016;144:574‑9.