



Indian J Dermatol. 2014 Nov-Dec; 59(6): 630.
doi: [10.4103/0019-5154.143526](https://doi.org/10.4103/0019-5154.143526)

PMCID: PMC4248517

Titanium Allergy: A Literature Review

[Manish Goutam](#), [Chandu Giriapura](#), [Sunil Kumar Mishra](#), and [Siddharth Gupta](#)

From the Department of Prosthodontics and Implantology, Rishiraj College of Dental Sciences and Research Centre, Bhopal, Madhya Pradesh, India

Address for correspondence: Dr. Manish Goutam, Post Graduate Student, Department of Maxillofacial Prosthodontics and Implantology, Rishiraj College of Dental Sciences and Research Centre, Bhopal – 462 036, Madhya Pradesh, India. E-mail: drmanishgoutam@yahoo.com

Received December 2013; Accepted February 2014.

Copyright : © Indian Journal of Dermatology

This is an open-access article distributed under the terms of the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Titanium has gained immense popularity and has successfully established itself as the material of choice for dental implants. In both medical and dental fields, titanium and its alloys have demonstrated success as biomedical devices. Owing to its high resistance to corrosion in a physiological environment and the excellent biocompatibility that gives it a passive, stable oxide film, titanium is considered the material of choice for intraosseous use. There are certain studies which show titanium as an allergen but the resources to diagnose titanium sensitivity are very limited. Attention is needed towards the development of new and precise method for early diagnosis of titanium allergy and also to find out the alternative biomaterial which can be used in place of titanium. A review of available articles from the Medline and PubMed database was done to find literature available regarding titanium allergy, its diagnosis and new alternative material for titanium.

Keywords: Allergy, contact dermatitis, lymphocyte transformation test, memory lymphocyte immunostimulation assay, polyetheretherketone, titanium

Introduction

What was known?

Titanium has been widely accepted as intraosseous implant material due to its excellent osseointegration and high resistance to corrosion.

Stainless steel was the first metallic biomaterial used successfully as an implant. Later, in 1932, the cobalt-based alloy named Vitallium was developed for medical applications. Titanium and its alloys in past few decades are widely used for dental implants and its prosthesis components. Commercially, pure titanium (CpTi) is used preferentially for endosseous dental implant applications. There are currently four CpTi grades and one titanium alloy specially made for dental implant applications. These metals are specified according to ASTM as grades 1 to 5. Grades 1 to 4 are unalloyed, while grade 5 is alloyed with 6% aluminum and 4% vanadium (Ti6Al4V), is the strongest.[1]

Titanium has high resistance to corrosion in a physiological environment and has an excellent biocompatibility that gives it a passive, stable oxide film; due to this reason, it is considered as the material of choice for intraosseous use in the medical field.[2,3,4,5] Apart from its success there are studies which show titanium as an allergen.[6,7,8]

An allergic reaction, or hypersensitization, is defined as an excessive immune reaction that occurs when coming into contact with a known antigen.[9] Titanium to provoke an allergic reaction, must have antigenic properties and must be in contact with the organism. The insertion of titanium implants and their permanence in the human body enhances the amount of internal exposure and it has been proven that titanium ions concentrate in tissues surrounding dental and orthopedic implants, as well as in regional lymph nodes and pulmonary tissue. Concentrations of between 100 and 300 ppm have been discovered in peri-implant tissues, often accompanied by discolorations.[10,11,12,13,14]

Attention is needed towards the development of new and precise method for early diagnosis of titanium allergy and also to find out the alternative biomaterial which can be used in place of titanium. A review of available articles from the Medline and PubMed database was done to find literature available regarding titanium allergy, its diagnosis and new alternative material for titanium.

Allergic reactions to titanium

In their ionic form, metals can be bonded with native proteins to form haptenic antigens, or can trigger the degranulation of mastocytes and basophiles, being capable of developing type I or type IV hypersensitive reactions.[15,16] Various allergic reactions to titanium mentioned in literature by many authors is listed in [Table 1](#). A synopsis of studies of proving allergy to titanium is given in [Table 2](#).

The orofacial regions have been associated with types I, III, and IV allergies. One of the most common types of allergy found in the oral cavity is type IV, in which the appearance of characteristic features related to the allergy, can start from a few days to several years from contact with allergens.[31]

Diagnostic test for allergy

Before implant placement It has been shown that many patients suffer from multiple allergies,[32] and that people with a history of allergy to metals or jewelry have a greater risk of developing a hypersensitivity reaction to a metal implant.[33] Furthermore, although titanium allergy has a low prevalence rate, for patients with a previous history of allergies, it may be advisable to carry out a metal allergy assessment and allergy testing before placing permanent implants, in order to avoid a failure of the implant due to an allergic reaction to titanium.

After implant placement The failure of implants has been widely studied, and the main causes of dental implant failure are infection and overload.[34,35,36] However, some failures are difficult to explain, such as spontaneous rapid exfoliation of the implant, or the successive failure of implants in the same patients, known as “cluster phenomenon”, without any infection or overload risk factor identified. Authors agree that in these cases, there must be a systemic determinant of failure that has not been identified or understood.[37,38]

An allergic reaction can be reasonably suspected after dental implant placement, on the basis of signs or symptoms associated with allergy, such as rash, urticaria, pruritus, swelling in the orofacial region, oral or facial erythema, eczematous lesions of the cheeks or hyperplastic lesions of soft tissue (the peri-implant mucosa).[24] In these cases, allergy testing should be performed.

Diagnostic tests for titanium allergy

Various diagnostic tests are available in the literature. It is difficult to compare the results from different studies related to titanium allergies, because some refer to the use of patch tests, while others use prick tests and/or blood tests.[39,40]

Patch test To date no standard patch test for titanium has so far been developed, and positive reactions to titanium have only rarely been demonstrated with skin testing.[32] The sensitivity of patch tests has been shown to be about 75% for type IV metal allergy. Some authors have suggested that 0.1% and 0.2% titanium sulfate solution and 0.1% and 0.2% titanium chloride are successful reagents for the skin-patch tests and could be a valuable alternative to the titanium oxide normally used for patch testing,[41] but so far no study related to dental implants allergies has used the method.

Memory lymphocyte immuno-stimulation assay test The MELISA test has been validated to detect

sensitization to titanium and other metals,[40] but there can be some lack of specificity in lymphocyte proliferation. It would be valuable to have a sensitive and specific test that could help in the diagnosis of titanium sensitization or allergy.

Blood test Helps in the diagnosis of a type IV allergy.

Lymphocyte transformation test *In vitro* testing with the Lymphocyte transformation test (LTT) measure lymphocyte proliferation following contact with an allergen is based on the tritiated thymidine incorporation by lymphocytes. Some authors report that there could be that non-relevant proliferation of lymphocytes happen in non-sensitized patients, leading to some false-positive results.

Future prospects in the diagnosis of sensitization or allergy to titanium

Interleukin-17 (IL-17) and Interleukin-22 (IL-22) are produced by a subset of a recently defined T-cell line, known as Th-17. IL-17 has been associated with many inflammatory diseases in humans, including rheumatoid arthritis, organ rejection and asthma. It has been showed that the number of Th-17 cells and the expression of IL-17 were significantly increased in positive patch test biopsies, regardless of the nature of the antigen.[42,43,44] IL-22 is a critical mediator in mucosal host defense, which has complex pro-inflammatory and anti-inflammatory and autoimmune effects. It has been shown that patients with contact dermatitis to nickel had a significantly higher IL-22 blood level, compared with control,[45] indicating a possible involvement of IL-22 in the pathogenesis of human allergic contact dermatitis.

It would be interesting to develop a blood test, based on the measurement of the production of IL-17 and/or IL-22 by lymphocytes, in order to be able to diagnose with certainty a sensitization to titanium.

Discussion

Investigations have been carried out about hypersensitivity reactions with titanium orthopedic implants; therefore it is not certain as to what extent the discoveries can be extrapolated to the oral cavity and dental implants. The intraosseus contact surface is smaller in dental implants than in orthopedic ones,[5,46] which may be particularly important considering that bone has a very low reactivity potential. On the other hand, oral mucosa and the skin behave very differently from an immunological point of view, partially because of the influence of specific immune systems for each organ, such as skin-associated lymphoid tissue and mucosa-associated lymphoid tissue. A practical application is that, in mucosa, the number of Langerhans' cells, which act as antigen-presenting cells, is much smaller.[15,21,47] It is because of this, and perhaps also because of its reduced permeability, that oral mucosa must be exposed to allergen concentrations 5-12 times greater than the skin in order to cause tissue microscopic reactions. Moreover, contact between the metal and the host is hampered, as the implant and prosthetic structures in the oral cavity are coated with a layer of salivary glycoprotein, which act as a protective barrier.[47]

It is important to recognize the difference between the presence of immunocompetent cells in tissues and clinical features consistent with hypersensitivity. In the future, our understanding of titanium allergy would be advanced by a comparison of histologic features in symptomatic and asymptomatic patients with titanium implants in the maxillofacial region. Sensitivity to titanium is characterized by the local presence of abundant macrophages and T lymphocytes and the absence of B lymphocytes, indicating Type 4 hypersensitivity. Researches are going on to develop a technique using flow cytometry, for the purpose of detecting the activation of lymphocytes stimulated by a metal, and measuring different mediators (cytokines, inflammatory mediators) released in response to the metal.

Evaluation of skin sensitization potential of nickel, chromium, titanium and zirconium salts done by Ikarashi *et al.*, [48] proved that a significantly large amount of titanium ion was required to elicit a skin reaction. The amount of titanium ion released from titanium alloys has been considered small because of the surface stabilization and the corrosion resistivity of titanium oxide formed on the surface of titanium alloys. These results may explain the rare case of contact sensitization to titanium.

Incidence of titanium sensitivity is increasing as its use in dentistry is increasing day by day. Research has now focused on designing alternative substitutes to titanium. One of the most promising novel materials is Polyetheretherketone (PEEK), which is a partially crystalline polyaromatic linear thermoplastic (typically of

30-35% crystallinity). PEEK offers a set of characteristics superior for biomaterials including excellent mechanical properties. Studies suggest that the implantable grade PEEK has bone forming capacity comparable to rough titanium.[49]

Conclusion

Improvements in health care and increased life expectancy of the population demand the design of implant biomaterials demonstrating no or minimal deleterious effects on host tissues. Although traditional materials, such as titanium or its alloys have been widely used and promote osseointegration, there are some concerns such as metal ion and debris release; allergic responses and sensitization. Better understanding and more research are necessary for acquainting the cause of allergy and development of new diagnostic tools for allergic reaction of Titanium. PEEK can be one of such alternatives which could provide a versatile foundation material that could be further suited to a particular purpose through readily tailoring its bulk or surface properties.

What is new?

Studies show that Titanium acts as a potential allergen, so diagnostic tests are mandatory before implant placements and more stress should be given to find new diagnostic tests as well as to design alternatives to Titanium such as PEEK.

Footnotes

Source of Support: Nil

Conflict of Interest: Nil.

References

1. Elias C, Lima J, Valiev R, Meyers M. Biomedical applications of titanium and its alloys. *J Miner Met Mater Soc.* 2008;60:46–9.
2. Smith D, Lugowski S, Mchugh A, Deporter D, Watson P, Chipman M. Systemic metal ion levels in dental implant patients. *Int J Oral Maxillofac Implants.* 1996;12:828–34. [PubMed: 9425764]
3. Sykaras N, Iacopino A, Marker V, Triplett R, Woody R. Implant materials, designs, and surface topographies: Their effect on osseointegration. A literature review. *Int J Oral Maxillofac Implants.* 1999;15:675–90. [PubMed: 11055135]
4. Frisken KW, Dandie GW, Lugowski S, Jordan G. A study of titanium release into body organs following the insertion of single threaded screw implants into the mandibles of sheep. *Aust Dent J.* 2002;47:214–7. [PubMed: 12405460]
5. Akagawa Y, Abe Y. Titanium: The ultimate solution or an evolutionary step? *Int J Prosthodont.* 2003;16(Suppl):28–9. [PubMed: 14661700]
6. Hensten-Pettersen A. Casting alloys: Side-effects. *Adv Dent Res.* 1992;6:38–43. [PubMed: 1292460]
7. Basketter DA, Whittle E, Monk B. Possible allergy to complex titanium salt. *Contact Dermatitis.* 2000;42:310–1. [PubMed: 10789872]
8. El Salam, El Askary. Oxford, UK: Blackwell Publishing Ltd; 2003. *Reconstructive Aesthetic Implant Surgery.*
9. Roitt IM, Delves PJ. 10th ed. London: Blackwell Science Ltd; 2001. *Essential Immunology.*
10. Parr GR, Gardner LK, Toth RW. Titanium: The mystery metal of implant dentistry. Dental materials aspects. *J Prosthet Dent.* 1985;54:410–4. [PubMed: 3864976]
11. Abdallah HI, Balsara RK, O’Riordan AC. Pacemaker contact sensitivity: Clinical recognition and management. *Ann Thorac Surg.* 1994;57:1017–8. [PubMed: 8166499]

12. Torgersen S, Gjerdet N, Erichsen E, Bang G. Metal particles and tissue changes adjacent to miniplates: A retrieval study. *Acta Odontol.* 1995;53:65–71.
13. Haug RH. Retention of asymptomatic bone plates used for orthognathic surgery and facial fractures. *J Oral Maxillofac Surg.* 1996;54:611–7. [PubMed: 8632246]
14. Matthew IR, Frame JW. Ultrastructural analysis of metal particles released from stainless steel and titanium miniplate components in an animal model. *J Oral Maxillofac Surg.* 1998;56:45–50. [PubMed: 9437981]
15. Schramm M, Pitto RP. Clinical relevance of allergological tests in total hip joint replacement. In: Willmann G, Zweymuller K, editors. *Bioceramics in Hip joint replacement.* New York, USA: Thieme; 2000. pp. 101–6.
16. Hallab N, Merritt K, Jacobs J. Metal sensitivity in patients with orthopaedic implants. *J Bone Joint Surg Am.* 2001;83:428–36. [PubMed: 11263649]
17. Lhotka C, Szekeres T, Fritzer-Szekeres M, Schwarz G, Steffan I, Maschke M, et al. Are allergic reactions to skin clips associated with delayed wound healing? *Am J Surg.* 1998;176:320–3. [PubMed: 9817247]
18. Valentine-Thon E, Schiwara HW. Validity of MELISA for metal sensitivity testing. *Neuro Endocrinol Lett.* 2003;24:57–64. [PubMed: 12743534]
19. Tamai K, Mitsumori M, Fujishiro S, Kokubo M, Ooya N, Nagata Y, et al. A case of allergic reaction to surgical metal clips inserted for postoperative boost irradiation in a patient undergoing breast-conserving therapy. *Breast Cancer.* 2001;8:90–2. [PubMed: 11180773]
20. Thomas P, Bandl WD, Maier S, Summer B, Przybilla B. Hypersensitivity to titanium osteosynthesis with impaired fracture healing, eczema, and T-cell hyperresponsiveness *in vitro*: Case report and review of the literature. *Contact Dermatitis.* 2006;55:199–202. [PubMed: 16958916]
21. Thomas P. Allergological aspects of implant biocompatibility. In: Willmann G, editor. *Bioceramics in Hip Joint Replacement: Proceedings 5th International Ceram Tec Symposium, Febr. 18/19, 2000;25 Tables.* New York: George Thieme Verlag; 2000. pp. 117–21.
22. Matthew I, Frame JW. Allergic responses to titanium. *J Oral Maxillofac Surg.* 1998;56:1466–7. [PubMed: 9846549]
23. Bircher AJ, Stern WB. Allergic contact dermatitis from ‘titanium’ spectacle frames. *Contact Dermatitis.* 2001;45:244–5. [PubMed: 11683844]
24. Mitchell DL, Synnott SA, Van Dercreek JA. Tissue reaction involving an intraoral skin graft and CP titanium abutments: A clinical report. *Int J Oral Maxillofac Implants.* 1990;5:79–84. [PubMed: 2202672]
25. Hunt J, Williams D, Ungersbock A, Perrin S. The effect of titanium debris on soft tissue response. *J Mater Sci Mater Med.* 1994;5:381–3.
26. Ungersboeck A, Geret V, Pohler O, Schuetz M, Wuest W. Tissue reaction to bone plates made of pure titanium: A prospective, quantitative clinical study. *J Mater Sci Mater Med.* 1995;6:223–9.
27. Lim H, Lee K, Koh Y, Park S. Allergic contact stomatitis caused by a titanium nitride-coated implant abutment: A clinical report. *J Prosthet Dent.* 2012;108:209–13. [PubMed: 23031726]
28. Lalor PA, Revell PA, Gray AB, Wright S, Railton GT, Freeman MA. Sensitivity to titanium. A cause of implant failure? *J Bone Joint Surge Br.* 1991;73:25–8.
29. Pigatto PD, Berti E, Spadari F, Bombeccari GP, Guzzi G. Exfoliative cheilitis associated with titanium dental implants and mercury amalgam. *J Dermatol Case Rep.* 2011;5:89–90. [PMCID: PMC3241953] [PubMed: 22408710]
30. Egusa H, Ko N, Shimazu T, Yatani H. Suspected association of an allergic reaction with titanium dental

implants: A clinical report. *J Prosthet Dent*. 2008;100:344–7. [PubMed: 18992567]

31. Chaturvedi TP. Allergy related to dental implant and its clinical significance. *Clin Cosmet Investig Dent*. 2013;5:57–61. [PMCID: PMC3753052]

32. Forte G, Petrucci F, Bocca B. Metal allergens of growing significance: Epidemiology, immunotoxicology, strategies for testing and prevention. *Inflamm Allergy*. 2008;7:1–18.

33. Hallab M, Mikecz K, Vermes C, Skipor A, Jacobs J. Differential lymphocyte reactivity to serum-derived metal-protein complexes produced from cobalt-based and titanium-based implant alloy degradation. *J Biomed Mater Res*. 2001;56:427–36. [PubMed: 11372061]

34. Esposito M, Hirsch J, Lekholm U, Thomsen P. Differential diagnosis and treatment strategies for biologic complications and failing oral implants: A review of the literature. *Int J Oral Maxillofac Implants*. 1999;14:473–90. [PubMed: 10453661]

35. Esposito M, Lausmaa J, Hirsch J, Thomsen P. Surface analysis of failed oral titanium implants. *J Biomed Mater Res*. 1999;48:559–68. [PubMed: 10421701]

36. Esposito M, Thomsen P, Ericson L, Lekholm U. Histopathologic observations on early oral implant failures. *Int J Oral Maxillofac Implants*. 1999;14:798–810. [PubMed: 10612916]

37. Wood M, Vermilyea S. A review of selected dental literature on evidence-based treatment planning for dental implants: Reports of the committee on research in fixed prosthodontics of the academy of fixed prosthodontics. *J Prosthet Dent*. 2004;94:447–62. [PubMed: 15523334]

38. Chuang S, Cai T, Douglass C, Wei L, Dodson T. Frailty approach for the analysis of clustered failure time observation in dental research. *J Dent Res*. 2005;84:54–8. [PubMed: 15615876]

39. Sicilia A, Cuesta S, Coma G, Guisasola C, Ruiz E, Maestro A. Titanium allergy in dental patients: A clinical study on 1500 consecutive patients. *Clin Oral Implants Res*. 2008;19:823–35. [PubMed: 18705814]

40. Müller K, Valentine-Thon E. Hypersensitivity to titanium: Clinical and laboratory evidence. *Neuro Endocrinol Lett*. 2006;27:31–5. [PubMed: 17261997]

41. Okamura T, Morimoto M, Fukushima D, Yamane G. A skin patch test for the diagnosis of titanium allergy. *J Dent Res*. 1999;78:1135.

42. Oboki K, Ohno T, Saito H, Nakae S. Th17 and allergy. *Allergol Int*. 2008;57:121–34. [PubMed: 18427165]

43. Zhao Y, Balato A, Fischelevich R, Chapoval A, Mann D, Gaspari A. Th17/Tc17 infiltration and associated cytokine gene expression in elicitation phase of allergic contact dermatitis. *Br J Dermatol*. 2009;161:1301–6. [PMCID: PMC3130797] [PubMed: 19785613]

44. Larsen J, Bonefeld C, Poulsen S, Geisler C. IL-23 and IL-17-mediated inflammation in human allergic contact dermatitis. *J Allergy Clin Immunol*. 2009;123:486–42. [PubMed: 18986691]

45. Ricciardi L, Minciullo P, Saitta P, Trombetta D, Saija A, Gangemi S. Increased serum levels of IL-22 in patients with nickel contact dermatitis. *Contact Dermatitis*. 2009;60:57–8. [PubMed: 19125725]

46. Brunski JB, Puleo DA, Nanci A. Biomaterials and biomechanics of oral and maxillofacial implants: Current status and future developments. *Int J Oral Maxillofac Implants*. 2000;15:15–46. [PubMed: 10697938]

47. Bass JK, Fine H, Cisneros GJ. Nickel hypersensitivity in the orthodontic patient. *Am J Orthod Dentofacial Orthop*. 1993;103:280–5. [PubMed: 8456786]

48. Ikarashi Y, Momma J, Tsuchiya T, Nakamura A. Evaluation of skin sensitization potential of nickel, chromium, titanium and zirconium salts using guinea-pigs and mice. *Biomaterials*. 1996;17:2103–8. [PubMed: 8902244]

49. Sagomonyants KB, Jarman-Smith ML, Devine JN, Aronow MS, Gronowicz GA. The *in vitro* response

of human osteoblasts to polyetherether ketone (PEEK) substrates compared to commercially pure titanium. *Biomaterials*. 2008;29:1563–72. [PubMed: 18199478]

Figures and Tables

Table 1

Authors	Allergic reactions
Hensten-Pettersen ^[6] (1992); Lhotka <i>et al.</i> ^[17] (1998); Valentine-Thon and Schiwara ^[18] (2003); Tamai <i>et al.</i> ^[19] (2001)	Urticaria, eczema, edema, redness and pruritus of the skin or mucosa, either localized, at distant sites, or generalized Atopic dermatitis
Thomas <i>et al.</i> ^[20] (2006)	Impaired healing of fractures
Haug <i>et al.</i> ^[13] (1996)	Pain, necrosis and weakening of orthopedic implants
Thomas <i>et al.</i> ^[21] (2000)	Tolerance phenomena
Matthew <i>et al.</i> ^[22] (1998); Bircher <i>et al.</i> ^[23] (2001)	Facial erythema
Mitchell <i>et al.</i> ^[24] (1990)	Non-keratinized, edematous, proliferative hyperplastic tissue

Allergic reactions to titanium

Table 2

Author	Study Summary	Outcome
Hunt <i>et al.</i> ^[25]	Examined tissues adjacent to titanium orthopedic fracture plates used for internal fixation of tibial fractures, removed 72 weeks after surgery	There was a chronic and sustained immune response to titanium. Macrophages and fibroblasts were the most abundant cells. An infiltrate of CD4 and CD8 positive lymphocytes suggested a delayed-type hypersensitivity reaction to titanium.
Ungersboeck <i>et al.</i> ^[26]	Compared the tissue response in both asymptomatic and symptomatic patients with titanium orthopedic bone plates used for fixation of long bone fractures	Light microscopy examination revealed a chronic granulomatous inflammatory reaction in tissues from patients complaining of persistent pain at the site of the fracture. There were significantly more lymphocytes and macrophages in the soft tissue covering the plate in symptomatic patients. In half of the symptomatic patients, there was localized tissue discoloration adjacent to screws and titanium was identified by atomic absorption analysis.
Torgersen <i>et al.</i> ^[12]	Studied the characteristics of immunocompetent cells in tissues adjacent to titanium and stainless steel "Champy" miniplates removed 24 weeks after fracture fixation	There was no difference in the incidence or distribution of immunocompetent cells adjacent to titanium or stainless steel miniplates. Metal particles were seen in both the soft tissue and the adjacent bone.
Lim <i>et al.</i> ^[27]	Studied allergic contact stomatitis caused by titanium nitride-coated implant abutment	Study clearly dictates the incidence of allergic contact stomatitis due to titanium nitride-coated implant abutment.
Lalor <i>et al.</i> ^[28]	Tissue samples removed from the joint capsule of five patients after hip revision surgery were examined by immunohistochemical methods	Hypersensitivity to titanium were reported. T cells and macrophages were present within the tissues, but there were few B cells or plasma cells, suggesting a cell-mediated immune response within the tissues adjacent to the prosthetic joints. Negative skin patch test results were obtained with dilute solutions of titanium salts in all five patients, but there were two positive skin patch tests with an ointment containing titanium. A proliferative soft tissue reaction adjacent to commercially pure titanium endosseous implant abutments has also been reported.
Pigatto <i>et al.</i> ^[29]	In a clinical case reported exfoliative cheilitis possibly caused by mercury-containing dental amalgam in close proximity to dental titanium implant in a 41-year-old woman	There was a strong temporal relation between last titanium dental implant and the onset of exfoliative cheilitis.
Egusa <i>et al.</i> ^[30]	A clinical case demonstrated the emergence of facial eczema in association with a titanium dental implant placed for a mandibular overdenture supported by 2 implants. Complete remission was achieved by the removal of the titanium material	This clinical report raises the possibility that in rare circumstances, for some patients, the use of titanium dental implants may induce an allergic reaction.

Synopsis of the studies related to titanium allergy

Articles from Indian Journal of Dermatology are provided here courtesy of **Medknow Publications**