Safety Controversies in Tooth Bleaching

Yiming Li, DDS, MSD, PhD[a,b,*]

KEYWORDS

• Peroxide • Safety • Toxicity • Tooth bleaching

In-office tooth bleaching has been a dental procedure for more than a century; however, at-home tooth bleaching was not available until 1989, when it was introduced by Haywood and Heymann.[1,2] With its demonstrated efficacy, lower cost than in-office bleaching, and the convenience of self-application, at-home bleaching quickly gained popularity and has now become an integrated procedure in aesthetic dentistry.[3] Nowadays, in addition to the bleaching products available from dental professionals, over-the-counter (OTC) and infomercial at-home bleaching products are available directly to consumers, and they can be applied with a custom or preformed tray, with a brush, or as a strip. In recent years, tooth bleaching similar to in-office procedures but performed under nondental settings, such as mall kiosks, spas, and cruise ships, has become available.[4]

Current tooth bleaching materials, whether used in office or at home, almost exclusively use peroxide compounds as the active ingredient, with carbamide peroxide and hydrogen peroxide (H_2O_2) being the most common.[2,5] Chemically, carbamide peroxide is composed of approximately 3.5 parts of H_2O_2 and 6.5 parts of urea, so that a bleaching material of 10% carbamide peroxide contains approximately 3.5% H_2O_2. Attempts were made to introduce at-home whiteners that claimed to contain no peroxide; however, such products did not gain acceptance because of the lack of evidence on their efficacy and controversy over their nonperoxide claim.[5] Typically, H_2O_2 concentrations of in-office bleaching products range from 25% to 38%, whereas at-home formulations contain 3.0% to 7.5% H_2O_2. However, in the recent years, there has been a trend of elevating the H_2O_2 concentration in at-home bleaching materials, and products containing up to 15% H_2O_2 have now become available directly to consumers for home use.

The efficacy of peroxide-containing tooth bleaching products has been debated. In general, data accumulated over the last 2 decades also suggest that tooth bleaching is

---

The author has nothing to disclose.

[a] Center for Dental Research, Loma Linda University School of Dentistry, 24876 Taylor Street, Loma Linda, CA 92350, USA

[b] Department of Microbiology and Molecular Genetics, Loma Linda University School of Medicine, Loma Linda, CA, USA

* Center for Dental Research, Loma Linda University School of Dentistry, 24876 Taylor Street, Loma Linda, CA 92350.

E-mail address: yli@llu.edu

Dent Clin N Am 55 (2011) 255–263

doi:10.1016/j.cden.2011.01.003 **dental.theclinics.com**

0011-8532/11/$ – see front matter

a relatively safe procedure. However, controversy concerning its safety has continued since the introduction of the home-use materials, and there have been reports of adverse effects of bleaching on oral tissues and restorative materials.[6–10] This article provides an overview of safety controversies in bleaching in relation to the biologic properties of H_2O_2 and discusses the proper use of bleaching to maximize benefits while minimizing potential risks.

BIOLOGICAL PROPERTIES OF H_2O_2 AND SAFETY CONCERNS WITH BLEACHING

H_2O_2 is a well-investigated chemical. It was discovered in 1818 and detected in human respiration in 1880. The well-known Fenton reaction was proposed in 1894. Peroxidase and catalase, which are 2 important enzymes in H_2O_2 metabolism, were discovered in 1898 and 1901, respectively. Shortly after the discovery of another enzyme, superoxide dismutase (SOD), in 1969, H_2O_2 was recognized as an important by-product in oxygen metabolism, and the research efforts on the biologic properties of H_2O_2 have been significantly increased since then.[2]

H_2O_2 is a normal intermediate metabolite in the human body, with a daily production of approximately 6.48 g in the liver. One of the key characteristics of H_2O_2 is its capability of producing free radicals, including hydroxyl radicals that have been implicated in various stages of carcinogenesis. Oxidative reactions of free radicals with proteins, lipids, and nucleic acids are thought to be involved in several potential pathologic consequences; the damage by oxidative free radicals may be associated with aging, stroke, and other degenerative diseases.[11,12] To prevent potential damage to cells during oxidative reactions and repair any damage sustained, there are various defensive mechanisms available at cellular and tissue levels. Enzymes such as catalase, SOD, peroxidase, and selenium-dependent glutathione peroxidase, which exist widely in body fluids, tissues, and organs, effectively metabolize H_2O_2.[13] Human saliva also contains these enzymes. In fact, salivary peroxidase has been suggested to be the body's most important and effective defense against the potential adverse effects of H_2O_2.[14] A study on infants, juveniles, adults, and adults with impaired salivary flow found rapid decomposition of H_2O_2 in dentifrices.[15] After brushing for 1 minute with 1 g dentifrice, less than 2% of the prebrushing dose of H_2O_2 (30 mg) was detectable in the oral cavity of the subjects.

Much of the safety concerns with home-use bleaching originate from H_2O_2 used in the materials, especially the known toxicology of free radicals. The oxidative reactions and subsequent damage in cells caused by free radicals are thought to be the major mechanisms responsible for the observed toxicity of H_2O_2. There have been concerns of potential systemic adverse effects if the bleaching material is ingested as well as local adverse effects on enamel, pulp, and gingiva because of the direct contact of the material with the tissues.[2] The safety controversies over peroxide-based tooth bleaching have prompted not only scientific deliberations but also legal challenges to its use in dentistry.[16,17]

CONCERNS WITH SYSTEMIC EFFECTS OF H_2O_2 IN BLEACHING

Considering the dosage and application mode of tooth bleaching, the exposure to the material during the bleaching procedure is inadequate to cause acute systemic toxicity. Although H_2O_2 is found to be mutagenic in the in vitro Ames test without S9 rat liver microsomes, it is not genotoxic in the same test when S9 is incorporated; it is not genotoxic in various animal models either.[2]

With the available data on the toxicity of H_2O_2 as well as the research on bleaching materials and the assessment of their exposure in bleaching, concerns with potential

systemic health risks have largely diminished, including the acute, subacute, and chronic toxicities associated with the use of materials containing 10% carbamide peroxide. This reduction is mainly because H_2O_2 exposure from bleaching is limited to the oral cavity and is incapable of reaching a systemic level. The possible exposure dose of H_2O_2 has been estimated at approximately 3.5 mg for a treatment of both arches with a whitener containing 10% carbamide peroxide,[2] whereas the oral cavity is capable of decomposing more than 29 mg H_2O_2 within 1 minute.[15]

CONTROVERSY OVER CARCINOGENICITY OF H_2O_2 IN BLEACHING

The issue of carcinogenicity of H_2O_2 is controversial in the literature, and the published results are contradictory in some studies.[17] Most studies found no evidence of carcinogenicity of H_2O_2; a few showed that H_2O_2 was anticarcinogenic, whereas several reported carcinogenicity or cocarcinogenicity of H_2O_2. The studies that have been cited most frequently as the evidence of carcinogenicity and cocarcinogenicity of H_2O_2 were reported by Ito and colleagues[18–20] and Weitzman and colleagues.[21] However, evaluation of these studies found significant deficiencies in design and conduct of the experiments as well as in the assessment of the results; consequently, the findings of these 4 studies were determined to be inadequate to substantiate their conclusions.[17]

It is obvious that the carcinogenic and cocarcinogenic potential of a tooth bleaching agent constitutes a significant health risk. Because of the potential significance of the study by Weitzman and colleagues,[21] which used local application of H_2O_2 on the oral mucosa of Syrian golden hamsters, the same study was repeated using proper design and methods; the results found no evidence of carcinogenicity or cocarcinogenicity of 3% H_2O_2.[22] Consequently, bleaching using 10% carbamide peroxide is regarded to be of no significant carcinogenic or cocarcinogenic risks. The overall data on bleaching obtained from more than 20 years also seem to support this conclusion. However, because of the significance of the carcinogenicity and relatively limited data available on the topic for bleaching, questions and debates over the carcinogenic risks of bleaching arise periodically. Future research is encouraged to help clarify the controversy and concerns with the topic.

POTENTIAL LOCAL ADVERSE EFFECTS ASSOCIATED WITH BLEACHING

Tooth bleaching requires direct contact of the material with the enamel surface. Although the gingival contact with the bleaching material is not intended, it often occurs when the material is applied at home by consumers. For some at-home systems, such as strips, the gingival contact is inevitable. Some bleaching regimens also involve a continued contact period of up to 7 to 8 hours (overnight). Consequently, possible adverse effects of bleaching on the enamel, pulp, and gingiva have been suggested and investigated.

Potential Adverse Effects on Enamel

The effects of bleaching on enamel were primarily examined in vitro using extracted human or bovine teeth. Bleaching seems to have minimal or no effects on enamel microhardness and mineral content; however, the results on enamel surface change are inconsistent.[23–26] Most scanning electron microscopic studies showed little or no morphologic changes of enamel surfaces associated with bleaching, whereas several studies reported significant alteration of enamel surfaces, including depression, porosity, and erosion, after bleaching. In most cases, however, the observed enamel surface alterations varied with the bleaching products used and seemed to

be associated with those patients using acidic prerinse or gels of low pH. The clinical relevancy of the observed changes in the enamel surface morphology has also been questioned. Studies have shown that some soft drinks and fruit juices are capable of causing comparable or greater demineralization and surface alteration of the enamel than those reported for bleaching agents.[26] To date, no clinical evidence of adverse effects of professional at-home bleaching systems on enamel has been reported; however, there have been 2 clinical cases of significant enamel damage associated with the use of OTC bleaching products.[6,7]

Potential Adverse Effects on Gingiva

H_2O_2 at high concentrations is an irritant and also cytotoxic.[2] In cell culture experiments, H_2O_2 is cytotoxic at concentrations ranging from 1.7 to 19.7 μg/mL (0.05–0.58 mmol/L).[27,28] At concentrations of 10% or more, H_2O_2 is potentially corrosive to the mucous membranes or skin, causing a burning sensation and tissue damage.[29] Studies also reported that commercial peroxide-based gels induced cytotoxicity.[29–32]

During the in-office bleaching procedure, which routinely involves the use of H_2O_2 at a concentration of 25% or more, adequate barriers are necessary to protect the gingiva from mucosal damage. If a leakage exists, serious tissue burn can occur. Because of this potential risk, local anesthesia should not be used for in-office bleaching, so that the patient can alert the dentist when the gel seeps through the barriers to cause a burning sensation or pain. However, simply relying on the patient's response is inadequate; clear instructions to the patient to report any discomfort, careful examination of the seal of the barrier after the gel application, and frequent monitoring of the seal throughout the bleaching process are all necessary to minimize the risk of gingival damage and irritation.

Gingival irritation is also common in at-home tooth bleaching. A study[33] found a higher (33.3%) prevalence of gingival irritation in patients using strips of 6.5% H_2O_2 compared with those using at-home tray bleaching with 10% carbamide peroxide (3.5% H_2O_2). A separate study[34] found that 50% of patients using the 6.5% H_2O_2 strips reported gingival irritation, which was about 3 times of those using the 5.3% strips (16.7%). These data indicate that the risk of gingival irritation in at-home bleaching is associated with the H_2O_2 concentration in the bleaching gel, that is, there is a higher prevalence of gingival irritation while using bleaching gels of higher peroxide concentrations. In most cases, the gingival irritation is mild to moderate, tends to be transient, and dissipates when the application discontinues. So far, studies on professional at-home bleaching reported no significant or permanent gingival damage.

Potential Adverse Effects on Pulp and the Risk of Tooth Sensitivity

Recent research, most of which used in vitro models, has shown that H_2O_2 in the bleaching gel applied on the enamel surface is capable of penetrating through the enamel and dentin to reach the pulp chamber.[35–39] An amount of less than 30 μg H_2O_2 may reach the pulp after the application of gels containing up to 12% H_2O_2 on the enamel surface for up to 7 hours. Although the amount of H_2O_2 detected in the pulp chamber tends to increase with the time and H_2O_2 concentration in the gel, such a relationship is not proportional. It was suggested that an amount of 50,000 μg H_2O_2 would be needed to inhibit pulpal enzymes,[40] so the detected amount of H_2O_2 that penetrated into the pulp chamber seems unlikely to cause significant damage to pulp tissues. However, there is a lack of in vivo studies on this topic, and long-term effects of such H_2O_2 exposure on pulp are yet to be determined.

Tooth sensitivity to temperature changes is a commonly observed clinical side effect in bleaching, and it has been suggested as an indication of possible pulp response to H_2O_2 that penetrates through the tooth hard tissue and reaches the pulp, although its mechanisms are not fully understood. Tooth sensitivity may or may not occur with gingival irritation.[41] In some cases, the patient may mistake gingival irritation for tooth sensitivity, or vice versa; therefore, careful examination and differential diagnosis are necessary for appropriate treatment regimens.

In general, up to 1 in 2 people may experience temporary tooth sensitivity as a result of tooth bleaching.[41–44] The development of tooth sensitivity does not seem to be related to the patient's age or sex, defective restorations, enamel-cementum abrasion, or the dental arch treated; however, the risk increases in patients with the frequency of daily application. The incidence and severity of the sensitivity may also depend on the quality of the bleaching material, the techniques used, and an individual's response to the bleaching treatment methods.[4] The sensitivity, usually mild and transient, often occurs during the early stages of tooth whitening, and for most patients it is tolerable to complete the treatment. So far, there are no reported cases of pulp necrosis caused by tooth bleaching; however, teeth with caries, with exposed dentin, in close proximity to pulp horns, or suspected to have cracks are potentially at risk for developing severe sensitivity and thus are not advisable for bleaching. In addition, defective restorations should be replaced before bleaching, and extra caution should be applied to children and adolescents because of their relatively larger pulp chamber.[45]

Potential Adverse Effects on Restorative Materials

Numerous studies have reported that tooth bleaching may adversely affect physical and/or chemical properties of restorative materials, including increased surface roughness, crack development, marginal breakdown, release of metallic ions, and decreased tooth-to-restoration bond strength. Potential adverse effects of bleaching on bonding strength have been well recognized.[9,46,47] A plausible mechanism is the inhibition of adequate polymerization of the bonding agent by the residual oxygen formed during bleaching. Similar effects are also applicable to other resin-based restorative materials that require in situ polymerization. The post-bleaching inhibitory effects on polymerization dissipate with time, and an interval of 2 weeks is found to be adequate to avoid such adverse effects.

A relevant safety concern is the mercury release from amalgam restorations during and after bleaching.[48–50] Although not much debate exists regarding whether bleaching causes mercury release, the reported amount of mercury release associated with bleaching varies greatly. The issue on potential health implications of the mercury released remains controversial and yet to be determined. Because of the known toxicity of mercury, as a general rule, it is not advisable to perform bleaching for those whose teeth are restored extensively with amalgam.

SAFETY CONCERNS WITH BLEACHING WITH NO INVOLVEMENT OF DENTAL PROFESSIONALS

Largely because of the clinically visible efficacy of at-home bleaching, an ever increasing number of OTC home bleaching products have become available directly to consumers shortly after the introduction of the night guard tray bleaching that was originally performed by dental professionals. There are various forms of these OTC bleaching products, including gels applied using a tray or paint-on brush, mouth rinses, chewing gums, toothpastes, and strips. Similar products are also available

through infomercials and the internet. More recently, tooth bleaching has become available in mall kiosks, salons, spas, and even cruise ships, which usually simulate the in-office bleaching settings, often involving the use of light but being performed by individuals with no formal dental training and not licensed to practice dentistry. This practice has come under scrutiny in several states and jurisdictions, resulting in actions to reserve the delivery of this service to dentists or appropriately supervised allied dental personnel.[4]

Basically, no scientific research is available on bleaching performed at mall kiosks, salons, spas, and cruise ships, whereas a significant amount of clinical data on the OTC bleaching products are available in the literature.[5,33,34,43] Overall, data indicate that adverse effects associated with the use of OTC bleaching products seem to be rare. There have been only 2 reports on irreversible enamel damage caused by OTC bleaching products.[6,7] However, it is unclear whether the low incidence of adverse effects associated with the use of the OTC bleaching products is the result of their low risk or the lack of means to detect and report adverse effects. The data available in the literature were collected from studies conducted by dental professionals, which were not intended for these OTC products. In addition, consumers are not generally aware of how to report adverse events through the US Food and Drug Administration's MedWatch system.[4] It is a reasonable assumption that when an individual purchases and uses an OTC bleaching product, some adverse effects, such as enamel surface changes, may go unnoticed; even those effects felt or detected by the user remain most likely unreported. More of a concern is the tendency of overusing or abusing an OTC bleaching product. Research efforts are encouraged to define the risks of OTC bleaching products, if any, under relevant scenarios intended for these products.

ROLES OF DENTAL PROFESSIONALS IN TOOTH BLEACHING

It is highly recommended that tooth bleaching involves dental professionals. Initial evaluation and examination of tooth discoloration are necessary for proper diagnosis and treatment; bleaching materials can affect restorative materials and may also result in color mismatch of teeth with existing restorations or crowns. Such evaluations cannot be performed or determined by consumers themselves or nondental individuals. Discoloration, particularly intrinsic stains, may not simply be an aesthetic problem,[5,51] and bleaching may not be the appropriate or the best choice for treatment. For at-home bleaching using trays, professionally fabricated, custom-fit trays reduce the amount of gel needed for maximal efficacy while minimizing the gel contact with gingiva. In addition, periodic evaluation of bleaching progress by dentists allows early detection of any possible side effects and reduces the risk of using poor-quality bleaching materials, inappropriate application procedures, and any temptation to overuse or abuse the product. The American Dental Association encourages all patients interested in tooth bleaching to seek advice from a dental professional.[4,52]

SUMMARY

Tooth bleaching is intended for improving tooth color and has become an accepted and popular dental procedure in aesthetic dentistry. Data accumulated over the last 20 years also indicate no significant, long-term oral or systemic health risks associated with professional at-home tooth bleaching using materials containing 10% carbamide peroxide, which is equivalent to 3.5% H_2O_2.

However, as with any dental procedure, bleaching involves risks. Tooth sensitivity and gingival irritation can occur in a significant portion of the patients, although in most cases they are mild to moderate and transient. When gels of

high H_2O_2 concentrations, such as those for in-office bleaching, are used without adequate gingival protection, severe mucosal damage can occur. Although rare, potential adverse effects are possible with inappropriate application, abuse, or the use of inappropriate at-home bleaching products. H_2O_2 is capable of producing various toxic effects, so that potential risks exist and need to be recognized. So far, little data are available on the safety of OTC at-home bleaching that simulates the intended application mode of these products, and the safety of bleaching performed at mall kiosks, salons, spas, and cruise ships is of particular concern because the procedure is similar to that of in-office bleaching but performed by nondental individuals.

Effective and safe tooth bleaching requires correct diagnosis of the problems associated with tooth discoloration or stains. Furthermore, tooth sensitivity and gingival irritation may occur during the course of bleaching treatment. To minimize risks and maximize benefits, the involvement of dental professionals in bleaching treatment is necessary.

REFERENCES

1. Haywood VB, Heymann HO. Nightguard vital bleaching. Quintessence Int 1989; 20:173–6.
2. Li Y. Biological properties of peroxide-containing tooth whiteners. Food Chem Toxicol 1996;34:887–904.
3. Kihn PW. Vital tooth whitening. Dent Clin North Am 2007;51:319–31.
4. American Dental Association (ADA). Tooth whitening/bleaching: treatment considerations for dentists and their patients. Chicago: ADA Council on Scientific Affairs; 2009.
5. Li Y. The safety of peroxide-containing at-home tooth whiteners. Compendium 2003;24:384–9.
6. Cubbon T, Ore D. Hard tissue and home tooth whiteners. CDS Rev 1991;84:32–5.
7. Hammel S. Do-it-yourself tooth whitening is risky. US News and World Report. April 2, 1998;66.
8. Dahl JE, Pallesen U. Tooth bleaching—a critical review of the biological aspects. Crit Rev Oral Biol Med 2003;14:292–304.
9. Attin T, Hannig C, Wiegand A, et al. Effect of bleaching on restorative materials and restorations—a systematic review. Dent Mater 2004;20:852–61.
10. Goldberg M, Grootveld M, Lynch E. Undesirable and adverse effects of tooth-whitening products: a review. Clin Oral Investig 2010;14:1–10.
11. Harman D. The aging process. Proc Natl Acad Sci U S A 1981;78:7124–32.
12. Lutz WK. Endogenous genotoxic agents and processes as a basis of spontaneous carcinogenesis. Mutat Res 1990;238:287–95.
13. Floyd RA. Role of oxygen free radicals in carcinogenesis and brain ischemia. FASEB J 1990;4:2587–97.
14. Carlsson J. Salivary peroxidase: an important part of our defense against oxygen toxicity. J Oral Pathol 1987;16:412–6.
15. Marshall MV, Gragg PP, Packman EW, et al. Hydrogen peroxide decomposition in the oral cavity. Am J Dent 2001;14:39–45.
16. Weiner ML, Freeman C, Trochimowicz H, et al. 13-week drinking water toxicity study of hydrogen peroxide with 6-week recovery period in catalase-deficient mice. Food Chem Toxicol 2000;38:607–15.
17. Li Y. Peroxide-containing tooth whiteners: an update on safety. Compend Contin Educ Dent 2000;21(Suppl 28):S4–9.

18. Ito A, Watanaee H, Naito M, et al. Induction of duodenal tumors in mice by oral administration of hydrogen peroxide. Gann 1981;72:174–5.
19. Ito A, Naito M, Naito Y, et al. Induction and characterization of gastro-duodenal lesions in mice given continuous oral administration of hydrogen peroxide. Gann 1982;73:315–22.
20. Ito A, Watanaee H, Naito M, et al. Correlation between induction of duodenal tumor by hydrogen peroxide and catalase activity in mice. Gann 1984;75:17–21.
21. Weitzman SA, Weitberg AB, Stossel TP, et al. Effects of hydrogen peroxide on oral carcinogenesis in hamsters. J Periodontol 1986;57:685–8.
22. Marshall MV, Kuhn JO, Torrey CF, et al. Hamster cheek pouch bioassay of dentifrices containing hydrogen peroxide and baking soda. J Am Coll Toxicol 1996;15: 45–61.
23. Rotstein I, Li Y. Tooth discoloration and bleaching. In: Ingle JI, Bakland LK, Baumgartner JC, editors. Ingle's endodontics. 6th edition. Hamilton (Canada): BC Decker Inc; 2008. p. 1383–99.
24. Potocnik I, Kosec L, Gaspersic D. Effect of 10% carbamide peroxide bleaching gel on enamel microhardness, microstructure, and mineral content. J Endod 2000;26:203–6.
25. White DJ, Kozak KM, Zoladz JR, et al. Peroxide interactions with hard tissues: effects on surface hardness and surface/subsurface ultrastructural properties. Compend Contin Educ Dent 2002;23:42–8.
26. Ren YF, Amin A, Malmstrom H. Effects of tooth whitening and orange juice on surface properties of dental enamel. J Dent 2009;37:424–31.
27. Grando LJ, Tames DR, Cardoso AC, et al. In vitro study of enamel erosion caused by soft drinks and lemon juice in deciduous teeth analyzed by stereomicroscopy and scanning electron microscopy. Caries Res 1996;30:373–8.
28. Ramp WK, Arnold RR, Russell JE, et al. Hydrogen peroxide inhibits glucose metabolism and collagen synthesis in bone. J Periodontol 1987;58:340–4.
29. Scientific Committee on Consumer Products (European Commission). Opinion on hydrogen peroxide in tooth whitening products. SCCP/0844/04. March 15, 2005.
30. Hanks CT, Fat JC, Wataha JC, et al. Cytotoxicity and dentin permeability of carbamide peroxide and hydrogen peroxide vital bleaching materials, in vitro. J Dent Res 1993;72:931–8.
31. Tse CS, Lynch E, Blake DR, et al. Is home tooth bleaching gel cytotoxic? J Esthet Dent 1991;3:162–8.
32. Woolverton CJ, Haywood VB, Heymann HO. Toxicity of two carbamide peroxide products used in nightguard vital bleaching. Am J Dent 1993;6:310–4.
33. Kugel G, Aboushala A, Zhou X, et al. Daily use of whitening strips on tetracycline-stained teeth: comparative results after 2 months. Compend Contin Educ Dent 2002;23:29–34.
34. Gerlach RW, Zhou X. Comparative clinical efficacy of two professional bleaching systems. Compend Contin Educ Dent 2002;23:35–41.
35. Thitinanthapan W, Satamanont P, Vongsavan N. In vitro penetration of the pulp chamber by three brands of carbamide peroxide. J Esthet Dent 1999;11:259–64.
36. Slezak B, Santarpia P, Xu T, et al. Safety profile of a new liquid whitening gel. Compend Contin Educ Dent 2002;23(Suppl 1):4–11.
37. Benetti AR, Valera MC, Mancini MN, et al. In vitro penetration of bleaching agents into the pulp chamber. Int Endod J 2004;37:120–4.
38. Pugh G, Zaidel L, Lin N, et al. High levels of hydrogen peroxide in overnight tooth-whitening formulas: effects on enamel and pulp. J Esthet Restor Dent 2005;17: 40–5.

39. Camargo SE, Cardoso PE, Valera MC, et al. Penetration of 35% hydrogen peroxide into the pulp chamber in bovine teeth after LED or Nd:YAG laser activation. Eur J Esthet Dent 2009;4:82–8.
40. Bowles WH, Ugwuneri Z. Pulp chamber penetration of hydrogen peroxide following vital bleaching procedures. J Endod 1987;8:875–7.
41. Leonard RH. Efficacy, longevity, side effects, and patient perceptions of nightguard vital bleaching. Compend Contin Educ Dent 1998;19:766–81.
42. Jorgensen MG, Carroll WB. Incidence of tooth sensitivity after home whitening treatment. J Am Dent Assoc 2002;133:1076–82.
43. Hasson H, Ismail AI, Neiva G. Home-based chemically-induced whitening of teeth in adults. Cochrane Database Syst Rev 2006;4:CD006202.
44. Burrows S. A review of the safety of tooth bleaching. Dent Update 2009;36:604–6, 608–10, 612–4.
45. Lee SS, Zhang W, Lee DH, et al. Tooth whitening in children and adolescents: a literature review. Pediatr Dent 2005;27:362–8.
46. Breschi L, Cadenaro M, Antoniolli F, et al. Extent of polymerization of dental bonding systems on bleached enamel. Am J Dent 2007;20:275–80.
47. Lima AF, Fonseca FM, Cavalcanti AN, et al. Effect of the diffusion of bleaching agents through enamel on dentin bonding at different depths. Am J Dent 2010; 23:113–5.
48. Rotstein I, Dogan H, Avron Y, et al. Mercury release from dental amalgam following treatment with 10% carbamide peroxide in vitro. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;89:216–9.
49. Rotstein I, Avron Y, Shemesh H, et al. Factors affecting mercury release from dental amalgam exposed to carbamide peroxide bleaching agent. Am J Dent 2004;17:347–50.
50. Al-Salehi SK. Effects of bleaching on mercury ion release from dental amalgam. J Dent Res 2009;88:239–43.
51. Shafer WG, Hine MG, Levy BM. Textbook of oral pathology. 4th edition. Philadelphia: WB Saunders; 1983. p. 766–8.
52. American Dental Association (ADA). For the dental patient: tooth whitening – what you should know. J Am Dent Assoc 2009;40:384.