

# A Review of Tooth Discoloration after Regenerative Endodontic Therapy

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## Abstract

**Introduction:** The American Association of Endodontists clinical considerations for regenerative therapy (April 2015) advise of the risk of the possible adverse effect of staining of teeth. It is widely acknowledged that before these guidelines were developed there was no standardized protocol for regenerative therapy, and different approaches using different materials have been reported. The purpose of this review was to undertake a systematic review of published cases to determine the incidence of reported discoloration and examine whether there was any particular association with any material. **Methods:** A PubMed search was performed using key words for regenerative endodontic therapy consistent with prior published systematic reviews. **Results:** There were 80 studies identified with 379 teeth treated. Many of the studies did not report on the presence or absence of discoloration. It was noted that there was a strong association of discoloration with the use of triple antibiotic paste containing minocycline; however, discoloration was also noted when other materials were used. Unfortunately, bleaching of stained teeth was not predictably achieved in some studies. **Conclusions:** The use of triple antibiotic paste with minocycline as the intracanal medicament should be reconsidered. Either calcium hydroxide or the double antibiotic paste of metronidazole and ciprofloxacin may limit discoloration. Mineral trioxide aggregate was also associated with discoloration. However, there is little evidence of an alternative superior material as a coronal barrier. Because discoloration is a patient-orientated outcome, further research should document and identify the incidence of discoloration in regenerative endodontic treatment. (*J Endod* 2016;42:563–569)

## Key Words

Discoloration, mineral trioxide aggregate, minocycline, regenerative endodontic therapy, revascularization, revitalization, triple antibiotic paste

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Regenerative endodontic therapy is an exciting and developing field in endodontics in which the treatment of immature permanent teeth with infected root canal systems using regenerative endodontic protocols often results in continued root maturation and apical closure. These protocols generally involve disinfection of the root canal and the introduction of a blood clot and/or stem/progenitor cells into the root canal space, which is then restored with a microorganism impregnable material, allowing tissue repair and further root maturation (1, 2). However, discoloration of the crown of the tooth is a reported unfavorable outcome associated with these techniques (3).

Earlier reports claimed discoloration was caused by the minocycline in the triple antibiotic paste (TAP) used in the disinfection phase (4, 5). Some studies then used other antibiotics not known to stain teeth (6, 7) or undertook single-visit techniques without the intracanal medicament phase (8). Calcium hydroxide, when used as an intracanal medicament, has also been shown to be associated with discoloration (9, 10). Chen et al (9) suggested that this discoloration may be caused by the presence of mineral trioxide aggregate (MTA) because both gray MTA (5) and white MTA (11) have been associated with discoloration. In a data analysis of clinical protocols, Kontakiotis et al (2) reported that MTA was used as the intracanal coronal barrier in 85% of the reviewed clinical studies. Furthermore, Diogenes et al (12) reported that TAP was used in 51% of reviewed clinical studies.

Berkhoff et al (13) evaluated the removal of TAP using different irrigation procedures and found that approximately 88% of TAP was retained in the root canal system regardless of the irrigation technique used and TAP was present circumferentially up to 350  $\mu\text{m}$  within the dentin. Conversely, up to 98% of the calcium hydroxide was removed and was only present in 50  $\mu\text{m}$  of dentin. In a spectrophotometric analysis of crown discoloration induced by various antibiotic pastes used in revascularization, TAP had a significant association with discoloration. However, calcium hydroxide showed no color changes exceeding the perceptibility threshold (14).

Variability of the clinical protocols applied during regenerative endodontic procedures is considerably high (2). A recent review also identified no clear consensus in treatment protocols yet stated only 2 studies reported tooth discoloration after the revascularization process (15). This finding is surprising and seems at odds with the many reports discussed previously that have outlined the subsequent discoloration of teeth after regenerative protocols and accordingly implicated various materials. This is a significant clinical problem because discoloration of teeth in particular has been related to a negative impact on the quality of life in adolescents, children, and their families (16–18) and thus should be considered as a “patient-oriented evidence measure” (19). The current American Association of Endodontists (AAE) clinical considerations for regenerative procedures also suggest that patients need to be advised of the risk of staining in the informed consent for the procedure and advocate the use of either calcium hydroxide or a low concentration of TAP and white MTA as the intracanal barrier (20). Measures suggested to prevent tooth staining include sealing the pulp chamber with a dentin bonding agent; delivering agents into the canal using a syringe; and, if TAP is used, ensuring that it remains below the cemento-enamel junction and using alternatives to MTA as the coronal barrier (20).

The purpose of this review was to undertake a literature review of studies in which regenerative endodontic protocols have been used to determine the number of studies that reported discoloration and to determine any associations with specific materials.

## Methodology

An electronic search was conducted using the PubMed database ([www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)) for publications on regenerative endodontics published up to June 30, 2015. The Medical Subject Headings used in the electronic search were “dental pulp,” “regenerative endodontic therapy,” “revascularization,” and “revitalization.” A significant article identified in the search reviewed the levels of evidence for the outcome of regenerative endodontic therapy and reported that there were 51 studies that included 255 treated teeth published between January 1993 and the second week of December 2013 (21). This included 2 high-level cohort studies, 8 case series, and 41 case reports. The inclusion criteria used were the following:

1. Clinical study related to the outcome of regenerative endodontic therapy in humans
2. Size of sample was given
3. The outcome was based on both clinical examination and radiographic interpretation
4. Adequate clinical and radiographic findings
5. Follow-up of at least 6 months
6. Articles presented in the English language

These criteria were adopted for the electronic search in the current study. All studies identified were read by both authors to determine whether discoloration was reported.

## Results

The electronic search identified 80 studies related to regenerative endodontic techniques, with 379 teeth treated. This included a further 29 studies and 124 treated teeth published since the analysis by Kontakiotis et al (21). However, it also included 4 studies that were published within their prescribed search dates.

Table 1 lists case series in which the presence or absence of discoloration after regenerative endodontic treatment has been reported, whereas Table 2 lists case reports in which the presence/absence of discoloration after regenerative treatment has been reported.

## Discussion

This study identified 80 studies related to regenerative endodontic techniques with 370 teeth treated. Kontakiotis et al (21) identified 51 studies (4, 5, 7–9, 11, 23, 27–40, 42, 48–74) that consisted of 2 high-level cohort studies (56, 73), 8 case series (ie, 6 or more cases reported) (9, 11, 23, 51, 55, 65, 67, 71), and 41 case reports with 255 treated teeth. In 2013, Diogenes et al (12) reported 34 studies with 152 treated teeth. The current study identified a further 30 studies (10, 22, 24–26, 43–47, 75–94), 3 of which (22, 75, 93) were in the time frame of Kontakiotis et al (21). Although the current study used identical inclusion criteria, the identification of the 3 additional studies may have been a difference in interpretation (67, 68, 93, 94) and that the inclusion of all the other identified studies by Kontakiotis (21) validated the current studies search methodology. Of the 30 additional studies, 7 were case series (10, 22, 24–26, 76, 87), with the remaining consisting of case reports. It is clear that there is continued reporting of teeth that have been treated with regenerative endodontic protocols, but the level of evidence of these studies remains low with case reports predominating the literature.

Table 1 includes case series in which the presence/absence of discoloration after regenerative treatment has been reported. Case series are considered a higher level of evidence than case reports (95). Of the 15 case series identified in this study, 8 reported discoloration after regenerative endodontic treatment. Two of these studies did not report how many teeth were discolored after regenerative endodontic treat-

ment, with Dabbagh et al not mentioning the number of discolored teeth in the 15 incisors out of the total of 18 treated teeth (22). Saoud et al also failed to identify the number of discolored teeth in the 20 anterior teeth treated but did state “many” were discolored (26). In the 6 case series that listed the discoloration of teeth after regenerative endodontic treatment, of 116 teeth, 42 incisor and 3 premolar teeth were noted to be discolored. The majority of these studies used TAP to medicate the canals. Nagata et al (10) medicated 12 incisor teeth with TAP and noted discoloration in 10, whereas of the 11 incisors medicated with calcium hydroxide and chlorhexidine, discoloration was only observed in 3 of the teeth. Chen et al (9) used calcium hydroxide and reported only 2 discolored teeth from 20 teeth treated. MTA was used as the coronal barrier in all of these case series studies. Finally, McTigue et al (23) described discoloration in 14 of 32 teeth treated. The initial high incidence of this adverse effect prompted the authors to use clindamycin to replace minocycline in the antibiotic paste and to use white MTA instead of the gray version. From these studies, it appears that teeth discolored with the use of both TAP and calcium hydroxide, although discoloration is less likely with the use of calcium hydroxide.

Thirty-one studies in which there was no postoperative clinical view or explicit statement in regard to the presence or absence of discoloration were identified. It is of note that of the 116 teeth treated, at least 60 were incisors. The majority of these studies medicated the canal with variations of TAP although calcium hydroxide (50, 55, 64, 85) and Odontopaste (ADM, Brisbane, Queensland, Australia) (77) were also used. Although the majority of these studies used MTA as the coronal barrier, glass ionomer cement (75, 77), Cavition (GC, Tokyo, Japan) (51), and calcium-enriched mixture cement (53) were also used. Because there was no postoperative clinical view or explicit statement on discoloration, no specific conclusion can be made on the use of these materials.

Nine studies in which preoperative discoloration was present but there was no discussion on whether teeth discolored further as a result of the regenerative treatment were identified. In these studies, 47 teeth were incisors with only 4 premolars treated. It is reasonable to assume that teeth that have been subjected to trauma, mostly incisors, would have discolored at the time of preoperative assessment. Again, the majority of the studies used TAP as the intracanal medicament with 1 study using formocresol (65). The majority of studies used MTA as the coronal barrier with only 2 studies using glass ionomer cement (65, 88).

Table 2 lists case reports in which the presence or absence of discoloration after regenerative treatment has been reported. These studies included 32 teeth, with 24 incisors, 1 canine, and 8 premolar teeth treated. The majority of the studies medicated the canals with TAP, but some studies used calcium hydroxide (33, 43), calcium hydroxide and iodoform compound (29), calcium hydroxide and chlorhexidine (35), calcium hydroxide and Augmentin (GlaxoSmith-Kline, Research Triangle Park, NC) (37), and calcium hydroxide and TAP (41). The majority of these studies used MTA as a coronal barrier although other studies used glass ionomer cement (29, 34).

Six case series and reports with clinical photographs taken at a review appointment without explicit indication of coronal discoloration at a follow-up appointment were identified. The studies treated 30 teeth; there were 27 premolars, 1 molar, and 1 canine. It may be that because only 1 of these teeth was an incisor that discoloration was not reported. Authors may not report results not favoring the test treatment and/or give scant attention to what they consider to be an unimportant result, with selective outcome reporting being a potential source of bias.

Kim et al (4) noted discoloration 6 weeks after the use of TAP. These authors then undertook an *in vitro* experiment with extracted human teeth and reported that minocycline, and not ciprofloxacin or metronidazole, was responsible for tooth discoloration. However,

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