Regenerative Endodontic Procedures: Clinical Outcomes

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KEYWORDS

• Revascularization • Regenerative endodontics • Immature teeth
• Root development • Revitalization

KEY POINTS

- Regenerative endodontic procedures (REPs) are stem cell–based procedures.
- Translational science has been crucial for the development of disinfection protocols that also foster stem cell survival and differentiation.
- Currently used REPs achieve both primary and secondary outcomes, healing of apical periodontitis and root development, respectively. However, prognostic factors that influence these outcomes remain largely unknown.
- Reestablishment of positive responses seen in vitality testing suggests directional targeting of apical neurons into the newly formed tissue.
- Current evidence suggests that REPs promote guided-endodontic repair (GER) as opposed to "true regeneration" of a pulp-dentin complex indistinguishable from the native pulp.

The field of regenerative endodontics has dramatically evolved in the past decade. The initial case report of a revascularization in 2001,[1] followed by another report in 2004,[2] captured the attention of endodontists worldwide. In addition to the resolution of apical periodontitis, there was evidence of unprecedented continued root development and reestablishment of vitality responses with these procedures. For the first time, successful clinical outcomes in teeth diagnosed with pulp necrosis were reported without the obturation of the root canal with an inert material (gutta-percha) or a bioceramic material (eg, mineral trioxide aggregate). This represented a departure from the classic philosophy that a root canal had to be sealed once debrided to achieve resolution of apical periodontitis and that reestablishment of physiologic pulp-like responses was possible. This truly represented a paradigm shift introducing endodontics to the fields of regenerative medicine and dentistry.[3] Suddenly, a significant

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body of basic science research related to dentinogenesis, tooth development, and mesenchymal stem cell biology was adopted by this emerging field and provided a foundation for further advancements and translation into clinical practice.

The goal of regenerative endodontics is the use of biologic-based procedures to arrest the disease process, preventing its recurrence while favoring the repair or replacement of damaged structures of the pulp-dentin complex. Therefore, regenerative endodontics includes both vital and nonvital pulp therapies. Although vital pulp therapies, such as direct and indirect pulp capping, and pulpotomy procedures aim to preserve and maintain pulpal health in teeth that have been exposed to trauma, caries, restorative procedures, and anatomic anomalies, nonvital therapies include procedures that aim to reestablish a new vital tissue to replace dental pulp lost to liquefaction necrosis following infection. Several terms have been coined for these procedures that include "revascularization,"[1] "revitalization,"[4,5] and "maturogenesis,"[6] among others. However, for the sake of this review, we focus on nonvital pulp therapies and address to these procedures collectively as regenerative endodontic procedures (REPs).

THE CLINICAL PROBLEM

Tooth development is a complex and long process of postnatal organogenesis. A tooth may take an additional 3 years after eruption to complete its development seen as complete root maturation.[7] The developing dentition is at risk for pulpal inflammation and necrosis due to trauma, caries, and developmental dental anomalies, such as dens evaginatus.[8–11] Loss of an immature permanent tooth in young patients with mixed dentition can be devastating, leading to loss of function; altered maxillary and mandibular bone development; interferences with phonetics, breathing, and mastication; and, importantly, there is a severe detrimental psychosocial effect on young patients.[12,13] Moreover, implants are contraindicated in patients undergoing cranioskeletal development, as their use has been associated with interferences in normal orofacial growth.[14] These teeth have been traditionally treated with apexification procedures using either long-term calcium hydroxide treatment[15,16] or immediate placement of a mineral trioxide aggregate (MTA) apical plug.[17] Although these treatments often result in the resolution of signs and symptoms of pathosis, they provide little to no benefit for continued root development,[18] remaining with thin fragile dentinal walls increasing susceptibility to fractures and lower survival.[15,19] A study evaluating root fractures after apexification procedures in 885 luxated nonvital incisors clearly demonstrated that as low as 28% and as high as 77% of the teeth had cervical root fractures owing to the least amount of dentin present in this area.[15] Therefore, clinicians must make use of all means necessary to retain the natural dentition through childhood and adolescence years, and hopefully beyond the maturation stage. To attain this goal, both vital pulp and nonvital pulp regenerative therapies should be considered.

It is important to note that most published regenerative endodontic cases, but not all,[20] report treatment outcomes in immature teeth with an open apex.[11] The degree of root formation and tooth maturation can be broadly classified according to previously established criteria (**Fig. 1**).[7,21,22] The great majority of cases treated with REPs are of teeth in stages 2 through 5, which include teeth with at least half of the root formed but with an open "blunderbuss" apex, or teeth that have achieved maximum root elongation but lack thickening of the dentinal wall and present with an open apex. As mentioned previously, the use of REPs in endodontics is not exclusive to immature teeth, because there have been cases published reporting