



Regenerative Endodontics: A Review of Literature

Sreedhara Y^{1*}, Singh N², Saraf S³, Tejani S⁴, Adhyapak A⁴ and Reddi GR⁴

¹Pediatric & Preventive Dentist, Kidz N Family Truesmile Dental, India

²Department of Periodontics & Implantology, G. Pulla Reddy Dental College and Hospital, India

³Pediatric & Preventive Dentist, Dr. Rachna's Smile Factory (KIDS), India

⁴Consultant Pediatric Dentist, India

***Corresponding author:** Yashwanth Sreedhara, Consultant Pediatric Dentist, Kidz N Family Truesmile Dental, Kurnool, India, Tel: 9494221375; Email: dryashwanthsreedhara@gmail.com

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Abstract

Until recent decades, apically immature necrotic teeth were indicative of apical growth. With advances in dentistry such as improved irrigation in procedures, better visualization of the surgical field, and advanced skills of endodontists, endodontic surgery has become the focus of attention. This review article addresses the tissue engineering, pulp regenerative strategies used in the past, current guidelines according to the American Endodontic Association, and future dental concepts.

Keywords: Regenerative Endodontic Procedures (REPs); Restoration; Non-Carious Cervical Lesions

Abbreviations

REPs: Regenerative Endodontic Procedures.

procedures designed to physiologically replace damaged tooth structures, including dentin and root structures, as well as cells of the pulp-dentin complex [1-3].

Introduction

This review describes the biological basis and clinical protocols that are used in regenerative endodontic procedures (REPs). Treatment for young permanent tooth with a necrotic root canal system and an incompletely developed root is very difficult.

Immature permanent teeth with necrotic pulp/ apical periodontitis are commonly treated with apexification procedure using $\text{Ca}(\text{OH})_2$ to induce apical MTA plug before root canal filling. Over an extended period of time, the $\text{Ca}(\text{OH})_2$ apexification procedure usually takes multiple treatment visits. Andreasen, et al. 2002 found that, prolonged exposure of immature permanent teeth with $\text{Ca}(\text{OH})_2$ dressing, which increases the risk of fracture [3-5].

Regenerative Endodontics: is defined as “biologically-based

Andreasen	An apical MTA plug is able to shorten the treatment time.
Rafter	The treatment outcome of $\text{Ca}(\text{OH})_2$ apexification and apical plug appears to be compatible [2,6,8].

Table 1: MTA vs $\text{Ca}(\text{OH})_2$.

Apexification procedure do have the potential to restore the vitality of damaged tissue in the canal space and promote root maturation of immature permanent teeth with necrotic pulp. Iwaya, et al. in 2001, introduced REVASCULARIZATION to treat an immature permanent tooth with apical periodontitis and sinus tract [1,2].

Regenerative Endodontic Treatment - Based on

➤ Cvek's Classification of Root Development

Stage	Description	Treatment Protocol
STAGE 1	Less than half of the root formation with open apex.	Regenerative endodontics
STAGE 2	Half of the root formation with open apex.	Regenerative endodontics
STAGE 3	Two-third of root development with open apex.	Regenerative endodontics
STAGE 4	Nearly completed root formation with open apex	Regenerative endodontics/ MTA plug and root canal filling

Table 2: Cvek's classification of root development [1,2,7].

Immature permanent teeth with a necrotic pulp requiring post for adequate coronal restoration are not suitable for RET and better treated with apical MTA plug and root canal filling.

Concepts in RET

Guided Tissue Regeneration: Blood as scaffold/ Blood clot induced [6,8,9].

Tissue Engineering: Synthetic biodegradable materials introduced as scaffolds for cell expansion.

Scaffolds used for RET

- **Based on origin:** Biological/ Natural [6,7].
- **Synthetic**

Polymers	Bioceramic
Poly(lactic acid (PLA)	Calcium phosphate materials
Poly-L-lactic acid (PLLA)	Bioactive glass
Polyglycolic acid (PGA)	Glass ceramics
Poly epsilon caprolactone (PCL)	

Table 4: Synthetic scaffolds.

Root Canal Disinfection

The important factors in the success of RET is preservation of stem cells. If infection is not under control, not only regeneration but also repair will not occur [2,3,8,13].

Effect of prior infection: It negatively affects the process of regeneration of pulp tissue by damage to tissue forming and stem cells in the periapical tissues.

For possible pulp tissue regeneration to occur in RET, intraradicular infection should be controlled.

Number of Visits

TWO VISITS: Mostly recommended by AAE, 2016 → With an intracanal medicament [5-7].

SINGLE VISIT: Recommended by Shin, et al. 2009; Chaniotis, 2016 → Without any intracanal medicament.

Platelet rich plasma
Platelet rich fibrin
Collagen
Chitosan
Glycosaminoglycans/ Hyaluronic acid
Demineralized or native dentin matrix
Blood clot
Silk

Table 3: Biological scaffolds.

Antiseptic Irrigants

Sodium hypochlorite is the most commonly used antiseptic irrigating solution in root canal therapy with concentrations 1-6% [2,3,8].

Sodium hypochlorite was found to be less effective in immature teeth when compared to mature teeth.

AAE clinical consideration for RET → Use of 1.5% sodium hypochlorite followed by 17% EDTA.

Calcium Hydroxide

- $\text{Ca}(\text{OH})_2$ is recommended as an intracanal medication in RET because of its good antimicrobial property [1,3,4,15].

- It can hydrolyze the lipid moiety of gram-negative bacterial lipopolysaccharide (LPS) → resulting in the release of FREE HYDROXY FATTY ACIDS and DEGRADATION OF LPS.

Root fracture following $\text{Ca}(\text{OH})_2$ as intracanal medicament	
Andreassen	Due to long term use.
Kahler	Related to root development stage than to the long term use of $\text{Ca}(\text{OH})_2$.

Table 6: Root fracture with intracanal medicament

➤ Intracanal Medicament

	Triple antibiotic paste	Augmentin
	(Minocycline, Ciprofloxacin, Metronidazole)	
Recommended by	AAE, 2016	Nosral, et al.
Description	It is recommended to use TAP at a conc. No greater than 1mg/ml in RET to avoid damage of stem cells from the apical papilla.	-Augmentin has been shown to kill 100% of microorganisms isolated from the infected root canal associated with an apical abscess.
		-Augmentin inhibits bacterial cell wall synthesis [2,3,5].

Table 7: Types of intracanal medicaments

Growth Factors

- Growth factors are polypeptides that are produced by immuno-inflammatory cells and tissue cells and bound to extracellular matrix.
- They regulate many aspects of cellular function including survival, b. proliferation, c. migration & d. differentiation
- They will determine the fate of stem/ progenitor cells and are often immobilized in scaffold to help promote tissue regeneration in tissue engineering.
- Galler, et al. 2015 → Medicaments and disinfectants used in RET influence the release of growth factors from dentine [5,7,9,10,12].

Blood Clot

-Intentional provocation of periapical tissue bleeding into canal space is done by induction of intra-canal bleeding in RET.

-Blood clot acts as a scaffold and helps in introducing platelet-derived growth factors mesenchymal stem cells into the canal space for possible regeneration of pulp tissue.

-After the recovery of periapical tissues from the severe injury, periapical bleeding induction can be done at the treatment visits or in the following visits [3,4,6,8,9].

Procedure for Regenerative Endodontic Treatment

First Appointment:

- Local anaesthesia, rubber dam isolation, access opening
- Canal irrigation with 20ml NaOCl [4-6,8].
- Dry canals with paper points.
- Intra-canal medicament placement
- $\text{Ca}(\text{OH})_2$ or
- TAP – seal till below CEJ, to avoid saining of crown
- Temporary cementation – Cavit/ IRM/ GIC
- Dismiss patient for 1-4 weeks

Second Appointment

- Assess response to initial treatment. If there are signs or symptoms of persistent infection, consider additional treatment with antimicrobial or alternative antimicrobial.
- Following irrigation and drying of canals with paper points, induce bleeding into the canal by over instrumentation
- Stop bleeding at the level that allows for 3-4 mm of restorative material.
- Place a resorbable matrix such as CollaPlug, Collacote, CollaTape or other material over the blood clot if necessary and white MTA/ $\text{Ca}(\text{OH})_2$ as capping material.
- A 3-4 mm layer of glass ionomer is flowed gently over the capping material and light-cured for 40s. To avoid discoloration of MTA, Biodentine is considered.

Anterior and premolar teeth	Molar teeth or teeth with PMF crown
Consider use of Collotape/ Collaplug and restoring with 3mm of RMGIC followed by bonding a filled composite to the beveled enamel margin.	Consider use of Collotape/ Collaplug and restoring with 3mm of MTA, followed by RMGIC or alloy.

Table 8: Matrix used in RET.

Follow up

- Clinical and radiographic exam.
- No pain, soft tissue or sinus tract (often observed between first and second appointments).
- Resolution of apical radiolucency (often observed 6-12 months after treatment).
- Increased width of root canals (this is generally observed before apparent increase in root length and often occur 12-24 months after treatment).
- Increased root length.

➤ Success of RET

Torabinajad et al, 2017 Tong et al, 2017	The success rate for resolution of periapical pathology as 91% with RET. Secondary outcomes → Increased root development -80% Apical closure -76%
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Table 9: Success of RET [7,8].

Management of immature permanent teeth after failed RET

- Treatment options: Non-surgical root canal therapy
- Regenerative endodontic retreatment Apexification [8-11].

Conclusion

This review of the literature suggests that RET may become the standard for the treatment of immature permanent teeth with necrotic pulp in the near future. Formation of living tissue in the root canal with stem cells, growth factors and scaffolds is a milestone in endodontics. However, this method requires further intensive research due to many controversial issues regarding clinical management and relatively poorly documented efficacy. In addition, it is necessary to develop an optimal treatment protocol for specific cases.

References

1. Nygaard-Ostby B, Hjortdal O (1971) Tissue formation in the root canal following pulp removal. *Scand J Dent Res* 79(5): 333-349.
2. Ostby BN (1961) The role of the blood clot in endodontic therapy. An experimental histologic study. *Acta Odontol Scand* 19: 324-353.
3. Kitasako Y, Shibata S, Pereira PN, Tagami J (2000) Short-term dentin bridging of mechanically-exposed pulps capped with adhesive resin systems. *Oper Dent* 25(3): 155-162.
4. Banchs F, Trope M (2004) Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol. *J Endod* 30(4): 196-200.
5. Torabinejad M, Turman M (2011) Revitalization of tooth with necrotic pulp and open apex by using platelet-rich plasma: a case report. *J Endod* 37(2): 265-268.
6. Martin DE, De Almeida JFA, Henry MA, Khaing ZZ, Schmidt CE, et al. (2014) Concentration-dependent effect of sodium hypochlorite on stem cells of apical papilla survival and differentiation. *J Endod* 40(1): 51-55.
7. Fagogeni I, Metlerska J, Lipski M, Falgowski T, Maciej G, et al. (2019) Materials used in regenerative endodontic procedures and their impact on tooth discoloration. *J Oral Sci* 61(3): 379-385.
8. Nakashima M, Iohara K (2014) Mobilized dental pulp stem cells for pulp regeneration: initiation of clinical trial. *J Endod* 40(4): 26-32.
9. Trevino EG, Patwardhan AN, Henry MA (2011) Effect of

irritants on the survival of human stem cells of the apical papilla in a platelet-rich plasma scaffold in human root tips. *J Endod* 37(8): 1109-1115.

10. Vishwanat L, Duong R, Takimoto K, Phillips L, Espitia CO, et al. (2017) Effect of bacterial biofilm on the osteogenic differentiation of stem cells of apical papilla. *Journal of Endodontics* 43(6): 916-922.
11. Zhujiang A, Kim SG (2016) Regenerative endodontic treatment of an immature necrotic molar with arrested root development using recombinant human platelet-derived growth factor: a case report. *Journal of Endodontics* 42(1): 72-75.
12. Nakahara T (2008) Tooth/periodontal organ engineering: the ultimate goal of tooth regeneration. In:

Tissue Engineering Research Trends, 1st (Edn.), Nova Science Publishers, USA, pp: 7-13.

13. Thibodeau B, Teixeira F, Yamauchi M, Caplan D, Trope M, et al. (2007) Pulp revascularization of immature dog teeth with apical periodontitis. *Journal of Endodontics* 33: 680-689.
14. Tong HJ, Rajan S, Bhujel N, Kang J, Duggal M, et al. (2017) Regenerative endodontic therapy in the management of nonvital immature permanent teeth: a systematic review – outcome evaluation and meta-analysis. *Journal of Endodontics* 43: 1453-1464.
15. Yang J-W, Zhang YF, Wan CY, Sun ZY, Nie S, et al. (2015) Autophagy in SDF-1 α -mediated DPSC migration and pulp regeneration. *Biomaterials* 44: 11-23.