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# Original Research

## Breaking New Ground in Endodontics: Regeneration Techniques Explored

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***ABSTRACT:***
Regenerative endodontics, an emerging field in dental science, focuses on revitalizing damaged dental tissues, including the dentin-pulp complex, and fostering tissue regeneration, rather than simply filling root canals. This review encompasses the evolution, methodologies, and clinical applications of regenerative endodontics, drawing on recent scientific advancements. Essential approaches, such as tissue engineering and scaffold utilization, are evaluated for their effectiveness in facilitating regenerative processes. Moreover, the review delves into growth factors, dental stem cells, and the role of biocompatible materials in enhancing outcomes. By examining both clinical success stories and challenges, this analysis illuminates the potential and limitations of regenerative endodontic treatments, offering insights into their role in modern dentistry. This comprehensive overview aims to elucidate the pivotal elements needed for successful tissue regeneration and inspire further research and innovation in this promising domain.
**Keywords:** Regenerative endodontics, Young permanent tooth, Dentin-pulp complex

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## INTRODUCTION

With the ability to encourage ongoing root formation and completion, regenerative endodontics has been heralded as an evolution for the management for developing permanent teeth with diseased canals in the root. In this sense, it is a fascinating evolving field. Calcium hydroxide or mineral trioxide aggregate (MTA) apexification has historically been used to cure young teeth with pulp necrosis.[1-3] This creates an apical calcific barrier that prevents future root growth, rendering the roots brittle and more prone to fracture and tooth loss. Regenerative endodontic treatments (REPs), which employ natural stem cells introduced into the tooth canal by slicing the periapical tissues to fill the canal with blood, have lately been suggested as a treatment option for young teeth with pulp necrosis.[2-5]

**History:**Dr B. W. Hermann (early 1960) derived the application of Calcium Hydroxide for vital pulp therapy.The experimental research of Nygaard-Ostby (1961) and Nygaard-Ostby & Hjortdal (1971) created the field of regenerative endodontics by creating bleeding from the periapical tissues into the partially filled root canal area of teeth that had been chemo-mechanically debrided. Rule DC in 1966 introduced double antibiotic paste. Hoshino in 1993 introduced triple antibiotic paste (TAP).Iwaya in 2001 introduced term ‘revascularization’. He also approaches to treat an immature permanent tooth with sinus tract infection and apical periodontitis by inducing intracanal hemorrhage.Banchs and Trope,2004: Provided evidence with a modified protocol of revascularization which include creating a blood clot in the canals following disinfection as a matrix for new tissue growth and a bacterial-tight coronal seal to prevent bacterial invasion into the pulp space.Nakashima & Akamine in 2005given the concept of the triad of tissue engineering.Murray et al. 2007 giventhe term ‘regenerative endodontics’ and was approved by the American Association of Endodontists (AAE) in 2007.Huang & Lin in 2008introduced the term‘revitalization’.The term ‘revitalization’ was approved by the European Society of Endodontology (ESE) position statement (ESE 2016).[6]

**Goals of Revascularization:**[7]
According to Banchs and Tropeand AAE described the followinggoals:

1. Eradication of the apical periodontitis, infection, and clinical symptoms.
2. The thickening of root dentinal walls and ongoing root completion.
3. Improvement in pulp vitality.

**Triad of tissue engineering**
Triad of regeneration involves stem cells, growth factors, and scaffold.

**Stem cells:** "Distinct subpopulation of undifferentiated cells with self-renewal and differentiation potential" is known as stem cells. Their environment and/or the cell communities encircling these maintain them in this stage, which is defined as undifferentiated cells which become privy to and react to the appropriate impulses. Being able to replicate itself for a long time and retain the ability to differentiate into several species for the length of the organism's life.[8]

**Types of stem cells**[8]

**a. According to their source:**

- Autologous cells: Derived from the individual in whom the transplant will be administered.
- Allogeneic cells: Derived from the same-species donor's body.
- Xenogeneic cells: Separated from members of a different species. For instance, heart implant construction uses animal cells.
- Syngeneic/isogenic cells: Isolated from genetically identical organisms. For instance, clones and twins.

**b. According to their potency:**

- Totipotent: Differentiable cells that can become new creatures. For instance, early embryonic cells.
- Pluripotent: Cells that can differentiate into almost any type of cell, but not an entire creature. For instance, blastocyst.
- Multipotent: Cells having a restricted variety of cell types during differentiation. For instance, dental pulp stem cells (DPSCs), cord blood, and fetal tissues

**c. Adult stem cells in the oral region:**

- SCAP: Stem cells of apical papilla
- iPACs: Inflammatory periapical progenitor cells
- DFSCs: Dental follicle stem cells
- DPSCs: Dental pulp stem cells
- PDLSCs: Periodontal ligament stem cells
- BMSCs: Bone marrow stem cells
- TGPCs: Tooth germ progenitor cells
- SGSCs: Salivary gland stem cells
- SHED: Stem cells from human exfoliated deciduous teeth
- OESCs: Oral epithelium derived stem cells
- GMSCs: Gingival derived mesenchymal stem cells
- PSCs: Periosteal derived stem cells

**Growth factors / Morphogens / Signaling Molecules:** These triggers cause certain mesenchymal stem cells to develop into odontoblast-like cells. Extended corticosteroid users show five times rise in the density of the predentin layer and a dramatic reduction in the radiographic volume of the pulp chamber. Dentin is believed to be a store of cytokines and growth factors. They facilitate revascularization, the proliferation of nearby cells, and the differentiation of certain cells along a predefined path. These odontoblast-produced growth factors and cytokines from the initial dentinogenesis are stored and calcified into the dentin after biomineralization.[1]
A wide range of growth factors include insulin-like growth factors (IGF-1, IGF-2), transforming growth factors β (TGF β-1, TGF β-2, and TGF β-3), growth hormone (paracrine/autocrine role), fibroblast growth factors (FGFs), tumor necrotic factors (TNFs), colony stimulating factors, interlukins, platelet derived growth factors (PDGF), and nerve growth factors (NGF). Morphogens comprises toll-like receptors (TLR-4 activated by lipopolysaccharides) and transcription factors MSX-1 and MSX-2, which regulate the second level.[1]

**Scaffold / Matrix Scaffold:** During cell growth and evolution, it produces a three-dimensional physiologic and physiochemical environment that promotes cell attachment and emigration. By arranging, directing, and providing both physical and chemical stimuli that offer the cell a precise geographical position and to regulate breakdown, modification, or proliferation while promoting gaseous and nutrient transfer, it is a tool that aids in cell development and differentiation. A perfect scaffold should be environmentally friendly, manually and structurally sufficiently strong to allow for the insertion of germinal agents and cells, be permeable to allow for the efficient movement of waste, oxygen, and nutrients, be recyclable and generate no contaminants, and allow for the placement of the regenerative cell while preserving the form and contours of the resulting tissue structure.[5]

**Types of scaffolds**[5]

**a. Biological/Natural:** Blood clot,platelet rich plasma (PRP),platelet rich fibrin (PRF),collagen, chitosan, glycosaminoglycans, demineralized dentine matrix.

**b. Synthetic/Artificial:** Polymers-Polylactic acid, polyglycolic acid, bioceramics like calcium, phosphate, bioactive glass, glass ceramics.

**Techniques of tissue engineering:**

1. **Root canal vascularization via blood clotting:**[1,9]When the roots are blunderbuss, it may be difficult to disinfect and shape the apical portion of the root canal. When root canals are being prepared or filled, the presence of thin, brittle dental walls may make them more likely to fracture and increase the danger of materials being extruded into the surrounding tissues. Clinical evaluation of a regenerative technique by theAAE:

**Case Selection:** Nonvital and immature tooth, final restoration that does not require post/core, cooperative patient/parent, not allergic to medicaments and antibiotics used in TAP (American Society of Anesthesiologists (ASA) 1 or 2).

**Informed Consent:** Information such as the need for a minimum of two visits, the use of antimicrobial agents, apparent tooth discoloration, lack of improvement after therapy, discomfort or contamination, various treatment methods such as apexification, no treatment, extraction, and authorization to proceed should all be included in informed consent.

**First Appointment:** After local anesthesia and access opening, isolation by rubber dam was completed. For thorough irrigation, use a side-vented needle and 20 milliliters of sodium hypochlorite (NaOCl). To reduce cytotoxic to stem cells in apical tissues, a lower dosage of 1.5% sodium hypochlorite (20 ml/canal for 5 min) is recommended, followed by irrigation with saline/EDTA (20 ml/canal for 5 min) using an irrigating needle inserted about 1 mm from the root end. SCAP survival is decreased with higher NaOCl concentrations. While 17% EDTA increases SCAP survival, 1.5% NaOCl has minimal negative effects on SCAP. Chlorhexidine should not be used for irrigation since it damages stem cells. The waterways are dried using paper points. According to the AAE protocol, triple antibiotic paste (TAP) should be used at a maximum concentration of 0.5 mg/ml to promote stem cell survival. Using a syringe, 0.1 mg/ml of metronidazole, ciprofloxacine, and minocycline are added to TAP in a 1:1:1 ratio. To reduce the chance of discoloration, pulp chamber can either remain beneath CEJ or be cured using a dentin bonding agent. Apply a coating of a temporary substance, such as glass-ionomer, Cavit, IRM, or a comparable substance, ranging from 3 to 4 mm. Give the patient a one- to four-week leave of absence.

**Second Appointment:** One to four weeks following the initial appointment is when it should happen. Assess the reaction to the initial treatment. Consider taking a different or extra antibiotic as part of your treatment if there are signs or symptoms of a recurring problem. 3% mepivacaine anesthesia without a vasoconstrictor and dental dam isolation are employed. Use twenty milliliters of 17% EDTA to irrigate thoroughly yet gently. In order to encourage bleeding into the canal space, excessive instrumentation (endo file, endo explore) and paper points are used to dry the canals. The goal is to rotate a pre-curved K-file two millimeters past the apical foramen in order to fill the canal with blood all the way to the cement-enamel junction. An efficient coronal seal is essential once the blood clot has formed. To serve as an internal matrix for the installation of around 3 mm of MTA and a layer of 3–4 mm GIC that was reinforced by composite bonding, a piece of premeasured Collaplug was placed on top of the blood clot.

**Follow-up:** The eradication of apical radiolucency (usually observed 6–12 months after therapy), wider root walls (usually observed 12–24 months after therapy; usually prior to apparent increase in root length), extended root length, positive pulp vitality test, and no signs of discomfort, swelling, or sinus tract were observed in the first and second appointments. A yearly follow-up is recommended at intervals of 6, 12, and 24 months after the first two years. A yearly follow-up is recommended following the first two years.

**Outcome Assessment:** Restoring pulp vitality and fostering ongoing root development are the objectives of REP. The radiographic root area increased by 31.6 percent after REP. For teeth treated with REPs, Chen et al. (2012) documented five different types of responses:

1. Deeper root canal walls and ongoing root development.
2. There is no discernible continuation of root growth, and the tips of the roots become tight and blunt.
3. Persistent root growth with an open apical foramen.
4. Severe canal space calcification.
5. A hard tissue barrier developed in the canal between the root apex and coronal MTA plus.

There aren't many vital pulp cells at the apical end, which could be a potential way for REPs to keep growing their roots. If the apical papillary tissues and HERs are destroyed, or if the transplantation of SCAP into the tissue lumen is the consequence of instrumentation that extends beyond the canal's apical limit, or if a blood clot can store growth factors like TGF and PDGF, these cells can divide and develop into odontoblasts under the guidance of intact HERs. It encourages the growth, maturation, and development of the undifferentiated progenitors of cementoblast, fibroblast, and odontoblast.

1. **Post natal stem cell therapy:**[10]In postnatal stem cell therapy, an infected root canal is injected with cells. Stem cells are divided into embryonic (pluripotent) cells that are isolated from

blastocyst is one of the kinds of stem cells in which all three germ layer derivatives can arise from them and postnatal cells that is taken from cord blood or bone marrow having less differentiation potential and are less malleable.

2. Stem cells of dental origin are:

- DPSCs: Dental repair is handled by DPSCs able to rebuild the pulp-dentin complex. SHED: Has the ability to develop into cells resembling odontonblasts, which create dentin-like structures.
- PDLSCs: Found in PDL that has been processed by enzymes. can create constructions resembling PDL or cementum.
- SCAP: Found at apices of growing teeth at junction of apical papilla and dental pulp. They can differentiate into odontoblastic, osteogenic, and neurogenic forms.

3. **Pulp implantation:**Pulp tissue produced in library is transferred to sterilized root canal. Sheets of biodegradable polymer nanofibers are used to create pulp tissue. (In vitro). To create 3-D pulp tissue, sheets are rolled together. This method's inability to guarantee whether cells are correctly affixed to the wall is a drawback.[10]
4. **Scaffold implantation:**An optimal scaffold should guarantee enough neurovascular supply to the newly formed pulp tissue during dental pulp regeneration. For instance, DPSCs are cultivated in vitro, implanted surgically, and seeded on a three-dimensional polyglycolic acid matrix.[10]
5. **Injectable scaffold delivery:**Injections are used to provide polymerizable hydrogel either alone or in combination with cell cultures. By acting as an extracellular matrix substitute, it might promote regeneration. Low cell survival rates and little control over tissue creation are disadvantages.[10]
6. **3-D cell printing:**By carefully positioning the cells, the created tissue resembles the structure of the dental pulp in its original state. Also help to replicate dental pulp tissue, layers of cells floating in hydrogel are dispersed using an inkjet equipment. Accurate three-dimensional models are needed for each pulp cavity and efficient delivery method.[10]
7. **Delivery of genes:** It is a method of introducing genes encoding growth factors, morphogens, and extracellular matrix components into a person's somatic cells, which has a therapeutic impact.[10]

**Complications:** The possible complications are discolouration due to minocycline, MTA material collapsing into the canal (Collaplug can be used to control this by maintaining it above the blood clot and waiting for at least fifteen minutes following the onset of bleeding), REPs cannot be used on teeth that require post retention in the canal space, rely on a blood clot, sometimes a canal develops total calcification, achieving the entire root length is challenging, development of bacterial strains that are resistant (caused by prolonged usage of antimicrobial drugs), hypersensitivity response to intracanal medication, necrosis could occur if the tissue becomes infected again.[1,11]

## CONCLUSION

Regenerative endodontics brings in a new era in physiological and therapeutic endodontics. This biologically based treatment is currently recognized as the first choice for treating young teeth with pulp necrosis due to the efficacy of multiple verified examples in studies. Our understanding of the clinical processes has expanded to encompass the release of growth factors that have solidified in the dentine walls, the stimulation of stem cell potential in the canal, and the elimination of pulp infection. Even though current procedures only achieve repair rather than genuine regeneration, more research in the field of stem cell-based pulp engineering is anticipated to enable real regeneration and better treatment outcomes.

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