Regenerative Endodontics: Regeneration or Repair?

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Abstract

Recent advances in biotechnology and translational research have made it possible to provide treatment modalities that protect the vital pulp, allow manipulation of reactionary and reparative dentinogenesis, and, more recently, permit revascularization of an infected root canal space. These approaches are referred to as regenerative procedures. The method currently used to determine the origin of the tissue secreted during the repair/regeneration process is largely based on the identification of cellular markers (usually proteins) left by cells that were responsible for this tissue production. The presence of these proteins in conjunction with other indicators of cellular behavior (especially biomineralization) and analysis of the structure of the newly generated tissue allow conclusions to be made of how it was formed. Thus far, it has not been possible to truly establish the biological mechanism controlling tertiary dentinogenesis. This article considers current therapeutic techniques to treat the dentin-pulp complex and contextualize them in terms of reparative and regenerative processes. Although it may be considered a semantic argument rather than a biological one, the definitions of regeneration and repair are explored to clarify our position in this era of regenerative endodontics. *(J Endod 2014;40:S70–S75)*

Key Words

Dentin bridge, endodontics, healing, regeneration, repair

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Significant progress in the field of prevention and treatment of pulpal and periradicular disease has led to an increasing amount of research into the role of the dentin-pulp complex and its ability to repair itself and regenerate mineralized tissue. For many years, research laboratories have investigated the pulp healing process with far reaching aims of enhancing its inherent regenerative capacity to completely regenerate this unique tissue. Recent advances in biotechnology and translational research have made it possible to provide treatment modalities that protect the vital pulp, allow manipulation of reactionary and reparative dentinogenesis, and, more recently, permit revascularization of an infected root canal space. Although the volume of the mature pulp is very small (less than 100 μL), it is conceivable that regeneration of such a small tissue should be relatively easy. Unfortunately, this is not the case. The dental pulp is a complex specialized connective tissue that is enclosed in a mineralized shell and has a limited blood supply; these are only a few of the many obstacles faced by the clinicians and researchers attempting to design new therapeutic strategies for its regeneration.

Regenerative endodontics should be considered as 2 entities. One is dentin-pulp complex regeneration (which could also be called dentin/odontoblast complex regeneration). This relates to preservation of pulp vitality and pulp capping. The second is dental pulp regeneration. This relates to regeneration of a vital tissue into an empty but infected root canal space.

Dentin-Pulp Complex Regeneration

Pulp capping and dentin bridge formation induction have been used for more than 70 years, with the first experimental studies published by Zander (1) in 1939. If the right environmental conditions persist, clinical results can be encouraging and tend to motivate the clinician to maintain pulp vitality as long as possible because of the advantages it can bring in terms of prolonging the life of the tooth. Nevertheless, high-quality robust clinical trials are lacking (2), and published findings are contradictory, not allowing for clear guidance for this clinical technique. A recent systematic review demonstrated success rates (pulp vitality maintained) at 3 years of 72.9% for pulp capping and 99.4% for partial pulpotomy (3). However, in a recent randomized clinical trial, Bjorndal et al (4) showed success rates to be much lower, 31.8% for pulp capping and 34.5% for partial pulpotomy.

Clinically, the aim of such treatment is to keep the pulp vital and maintain its homeostatic functions, thus avoiding pulpectomy or extraction of the tooth. Success of the treatment is assessed by the symptoms reported by the patients and through the use of relatively rudimentary investigations such as thermal tests, electrical tests, tenderness to percussion or palpation, and radiographic assessment. It has been well-established that clinical signs and symptoms do not correlate to the histologic status of the tooth (5). Biological research methods allow for more sophisticated assessment and enable the researcher to observe and analyze the histologic structure, cell behavior, and immunologic/inflammation status of the tissue concerned. Such techniques allow the pulpal responses to be assessed with greater accuracy than in clinical studies. To study the physiological and reparative processes of the pulp, *in vitro* experiments with immortalized cells or primary cell cultures can be used. The limitations of these studies must be acknowledged; they can only mimic biological processes such as mineral production and cannot prove conclusively the type of mineralized tissue formed. Frequently these experiments are supported with gene expression data to establish the likely gene regulation that induced this mineral production. Until phenotypic markers associated with dentin production are shown,

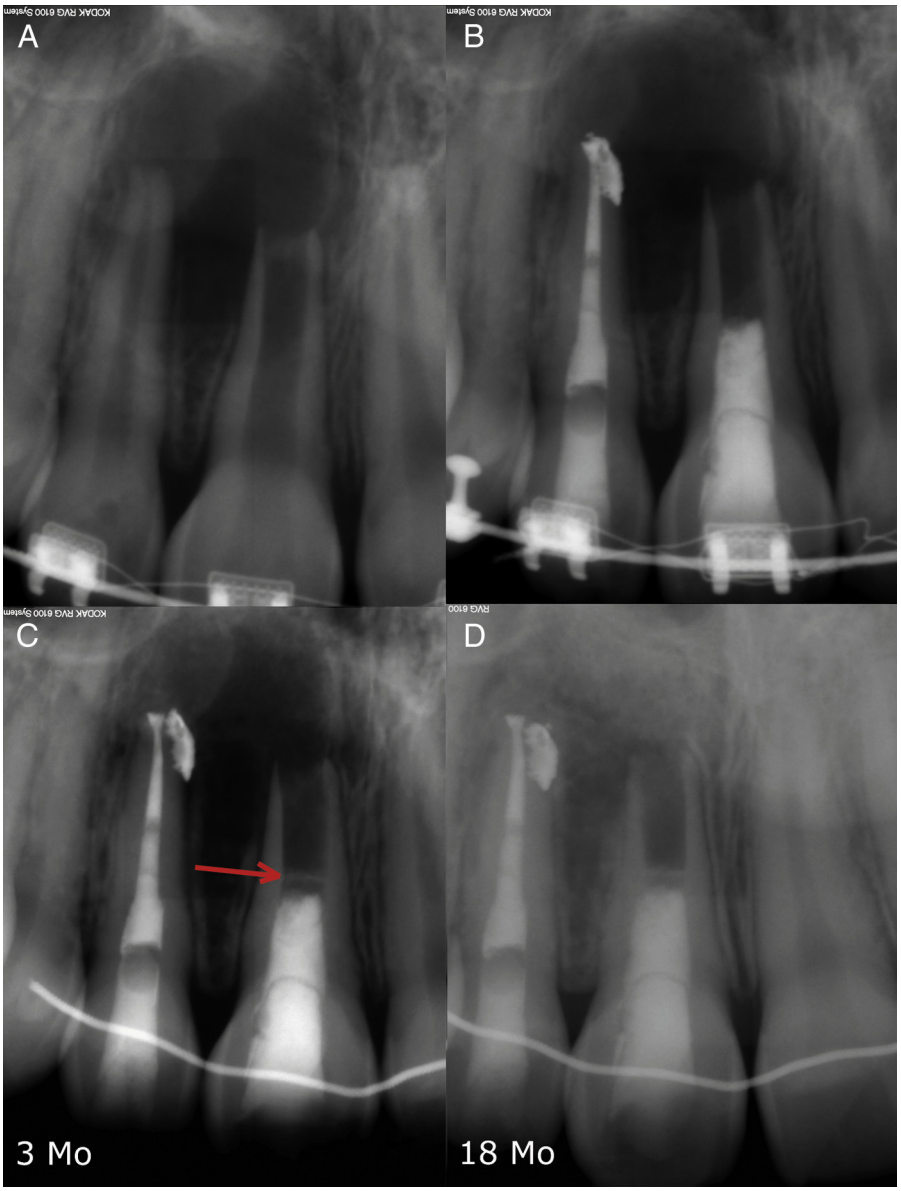

Figure 1. (*A* and *B*) Endodontic treatment by revascularization on tooth #8 of a 16-year-old girl. Note formation of a mineralized barrier distant from coronal filling material (mineral trioxide aggregate) (*arrow*) (*C*). At 18-month recall, the bone healing is complete, and the mineral barrier is still present (*D*). Nevertheless, no root lengthening or apexogenesis is noticeable.

the results are often viewed with skepticism to whether the mineral tissue formed is from odontoblastic origin.

Regeneration/Repair and Remodeling

Bone is constantly being remodeled, and newly generated tissue is replaced within a few months by new bone. The turnover of bone means that gradually the newly secreted tissue will merge with other tissue laid down at different times, and new and old tissue becomes homogenous. Some exceptions remain, for example as in the case of pseudarthrosis. This new non-resident tissue would be known as reparative tissue and be considered distinctly different from that of tissue that has formed through the process of regeneration. Remodeling can also be at the origin of destruction of regenerated tissue (partial or complete), if this one is not biologically identical to the original one (6).

Remodeling of dentin does not occur, and newly formed tissue will never be replaced. Histologically, tertiary dentin can appear to be similar to secondary dentin; however, it is never truly the same and does not form a continuum with preexisting dentin.

From a semantic point of view, it may be pertinent to consider the union of pulp and dentin differently and think of the tissue as the dentin-odontoblastic complex rather than the dentin-pulp complex. Dentin is uniquely penetrated by odontoblast processes that form an intimate and cohesive union with the underlying odontoblastic palisade. This layer could be regarded as a membrane that separates itself from the pulp underneath by the acellular layer of Weil. A breakage in this odontoblastic membrane due to caries, trauma, or iatrogenic damage results in exposure of the pulp tissue itself, leaving it unprotected and vulnerable.

The method currently used to determine the origin of the tissue secreted by the processes of repair/regeneration is generally based on cellular markers (usually proteins) left by cells that were responsible