

Pulp regeneration after non-infected and infected necrosis, what type of tissue do we want? A review

REVIEW ARTICLE

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Abstract – Regeneration (revitalization) of infected necrotic pulp tissue has been an important issue in endodontics for more than a decade. Based on a series of case reports, there appears to be evidence that new soft tissue can enter the root canal with a potential for subsequent hard tissue deposition resulting in a narrowing of the root canal. Very little is presently known about the exact nature of this tissue growing into the canal and how it may behave in the long term. In the case of regeneration of necrotic non-infected pulp tissue, a series of clinical and histological studies have shown that such events may take place in four variants: (i) Revascularization of the pulp with accelerated dentin formation leading to pulp canal obliteration. This event has a good long-term prognosis. (ii) Ingrowth of cementum and periodontal ligament (PDL). The long-term prognosis for this event is not known. (iii) Ingrowth of cementum, PDL, and bone. The long-term prognosis is only partly known, but cases developing an internal ankylosis have been described. (iv) Ingrowth of bone and bone marrow is a rare phenomenon and the long-term prognosis does not appear to be good. Based on current knowledge, expectations with respect to pulp regeneration (revitalization) of infected necrotic dental pulps are difficult to predict; more information than now available is needed before procedures for pulpal regeneration can be routinely recommended with a predictable long-term prognosis.

Necrosis of a dental pulp can be either infected or non-infected. In recent years, much effort has been invested in finding alternatives to conventional endodontic procedures for teeth with immature roots that have developed infected pulp necrosis; pulp regeneration has received much attention in such cases (1–6). This effort has, as reported in a few studies and case reports, led to procedures for stimulating ingrowth of tissues into pulp spaces followed after some time in a radiographically observable hard tissue deposition in the root canals (1, 7–22).

In an experimental study in dogs, it was shown that the ingrowth of new tissue in most cases had little similarity to ordinary pulp tissue and in some cases looked like a mixture of cementum, periodontal ligament (PDL), and bone (12, 23). Such findings raise the question: Are we 'regenerating' or 'repairing' diseased pulp tissue? In that regard, it may be useful to consider the classical definition of these two healing events, where regeneration is defined as the biologic process by which the structure and function of the disrupted or lost tissue is completely restored, whereas repair is a biologic process whereby the continuity of disrupted or lost tissue is renewed by new tissue that does not restore structure or function (i.e. scar tissue) (24). Throughout this article, these definitions will be adhered to when

characterizing the tissues recruited for the pulp space either after dental trauma events with ensuing non-infected pulp necrosis or after pulp extirpation in case of infected pulp necrosis.

In the early 1960s, Nygaard-Östby and coworkers performed some clinical experimentations in humans in which infected root canals were debrided and disinfected followed by subsequent attempts at pulpal healing by mechanically creating a blood clot in the canals (25–27). The findings showed that ingrowth was possible to a certain extent, but the new tissue that formed had no similarity to normal pulpal tissue. In most cases, it consisted of strands of fibrous tissue along with resorption of the root canal walls and sometimes deposition of cementum-like tissue.

One may ask what type of replacement tissue is optimal for occupying the pulp space (28). Before answering that, it may be appropriate to ask why one would want to change a hitherto well-accepted endodontic approach to the treatment of an infected root canal in a tooth with immature root formation. One answer relates to the disadvantages of the present calcium hydroxide (Ca(OH)₂) apexification technique:

- 1 It is a very lengthy procedure often requiring 1–2 years of treatment (29, 30).

- 2 The use of $\text{Ca}(\text{OH})_2$ has been shown both in clinical studies (31, 32) and in experimental studies (33, 34) to lead to a weakening of the root structure, often resulting in cervical root fractures (Fig. 1).

The latter finding in particular points to a need for alternative endodontic procedures such as pulp revitalization after pulp necrosis in incompletely developed teeth. In that regard, attempts to avoid long-term use of $\text{Ca}(\text{OH})_2$ are indicated, and if at the same time the ingrowing soft tissues have the capacity to form new hard tissue inside the root canal and thereby strengthening the root structure, this would be a desirable outcome and could improve long-term prognosis for the involved teeth.

Evaluation of treatment goal

The purpose of attempting ingrowth of new soft tissue into the pulp space is threefold:

- 1 To create (regenerate) the presence of new pulpal tissue.
- 2 To shorten the treatment time that it takes using $\text{Ca}(\text{OH})_2$ to induce apexification, followed by root canal filling.
- 3 To reduce the brittleness of the root dentin caused by the use of $\text{Ca}(\text{OH})_2$.

The two last points are self-evident, but the first one needs to be examined. Ideally, it would be optimal to have new pulpal tissue that could deposit new hard tissue on the canal walls thus increasing the strength of the tooth. Secondly, a new pulp could reproduce pulpal responses such as tertiary dentin production when stimulated by bacterial invasion of dentin tubules or dentin exposure owing to attrition. It would certainly be desirable if the hard tissue formed by the new pulpal tissue was similar to original dentin with associated odontoblasts capable of responding to various stimuli. The reported regeneration (revitalization) studies to date, however, have not provided precise information about a hard tissue with the classical pulp-odontoblast-dentin relationship. Instead, cases with cementum or bone-like tissue formation in the pulp spaces have been described (12, 23). This naturally raises the question about how these types of different tissues will behave inside a root canal over time. The answer to this question has so far not been presented.

There is information from various research reports that may provide some insight into the possible behavior over time when cementum, PDL, and bone are present in

the root canal. This information comes from a series of dental trauma situations and tooth autotransplantation cases. In this context, it should be noted that these healing events all occurred under non-infected pulp necrosis conditions. Based on the analysis of long-term follow up of 1200 traumatized teeth (root fractures, luxation injuries, and replanted avulsed teeth) (35–41) and 370 autotransplanted premolars (42, 43), as well as experimental studies in monkeys (44, 45), four different pulpal healing outcomes have been documented after such events.

These responses can be categorized into the following healing scenarios according to the type of tissues growing into the root canal:

- 1 Revascularization of the pulp with accelerated dentin formation leading to pulp canal obliteration (PCO).
- 2 Ingrowth of cementum and PDL.
- 3 Ingrowth of cementum, PDL, and bone.
- 4 Ingrowth of bone and bone marrow.

It would appear from these four healing scenarios that different cell populations invade the pulp spaces after trauma or transplantation. In the following, an analysis will be made about the stability of these four healing scenarios over time, i.e. do they lead to a secondary pulp necrosis (in case of PCO), to internal repair-related root resorption (internal surface resorption), or to internal ankylosis-related (replacement) resorption? The latter is manifested by a failure of the tooth to erupt normally.

Revascularization of the pulpal tissue with accelerated dentin formation and PCO

This event usually occurs after severance of the apical neurovascular supply to the pulp and is therefore primarily associated with luxation injuries with displacement, (extrusive, lateral, and intrusive luxation) and avulsion with subsequent replantation (Fig. 2) (46). The cause of this outcome is possibly related to the lack of complete nerve regeneration in the healing pulp, a finding that is strongly related to odontoblastic activity (46). Pulp canal obliteration almost always leads to a color change in the crown (becoming more opaque and yellow) and carries a 1% yearly risk of developing apical lesions of endodontic origin. The latter phenomenon is possibly related to the very narrow apical foramen in teeth with PCO where just a minor new trauma may lead to renewed severances of the neurovascular supply, or a carious attack, or crown preparation, or

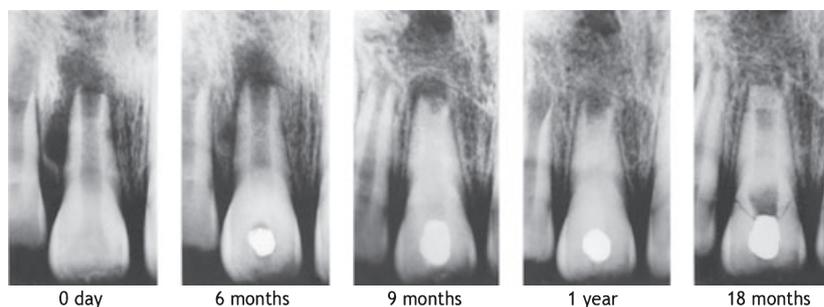


Fig. 1. The use of calcium hydroxide to disinfect the root canal and induce closure of the apical foramen in a central incisor appears to have weakened the root structure leading to cervical fracture from minor trauma. From Cvek (30).

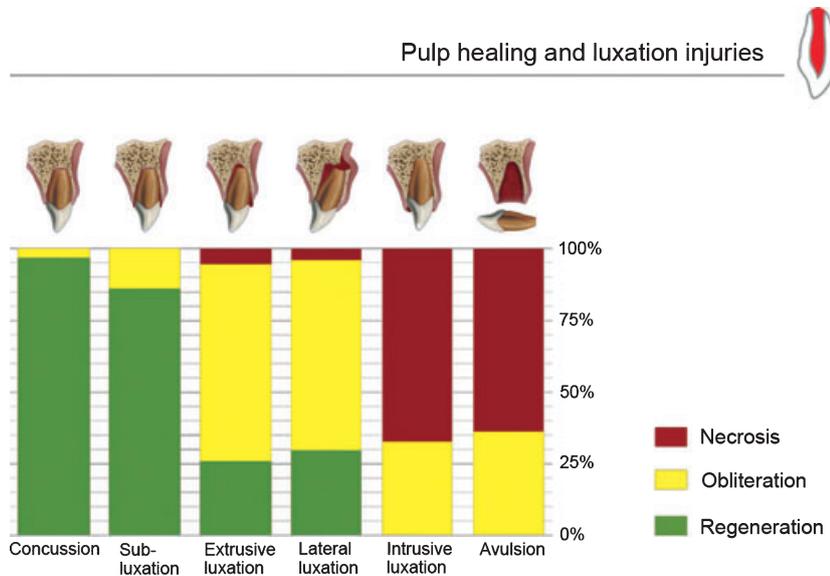


Fig. 2. Frequency of pulp canal obliteration in teeth with incomplete root formation and various luxation type injuries. From Andreasen, Malmgren & Tsilingaridis (in preparation).

development of crown infractions that may lead to bacterial invasion in a much compromised pulp with reduced vascularity (47).

Ingrowth of cementum and PDL into the pulp space

This type of tissue has been found in the coronal segment of root-fractured teeth after pulpal revascularization (Andreasen & Bakland, in preparation). Owing to continuous cementum deposition, a PCO situation may occur. Whether this implies a risk of future pulp necrosis is presently not known.

Ingrowth of cementum, PDL, and bone into the pulp space

This phenomenon has been known for some time to occur after dental trauma (48, 49) (Fig. 3). The event apparently takes place when Hertwig’s epithelial root sheath has been damaged during a luxation injury, or

when an avulsed tooth has been stored improperly before replantation (39), or when a pulp canal is wide open and the tooth is not properly repositioned (38). This latter phenomenon indicates that Hertwig’s epithelial root sheath deteriorates resulting in bone, cementum, and PDL-derived cells entering the pulp cavity whereby an internal PDL development takes place (50) (Andreasen, Malmgren & Tsilingaridis, in preparation; Malmgren, Tsilingaridis & Andreasen, in preparation). This phenomenon was found to take place in lateral luxation and intrusion cases (6% and 7%, respectively) and in 10% of replantation of avulsed teeth and in all these instances in teeth with immature root formation (Fig. 4). It is presently not known how many of these cases will present long-term problems in relation to development of internal ankylosis-related resorption from the presence of bone inside the root canal (Fig. 5). A recent histological study of 22 cases has however shown that such events may happen (Malmgren, Tsilingaridis & Andreasen, in preparation). The ankylosis sites usually appear in

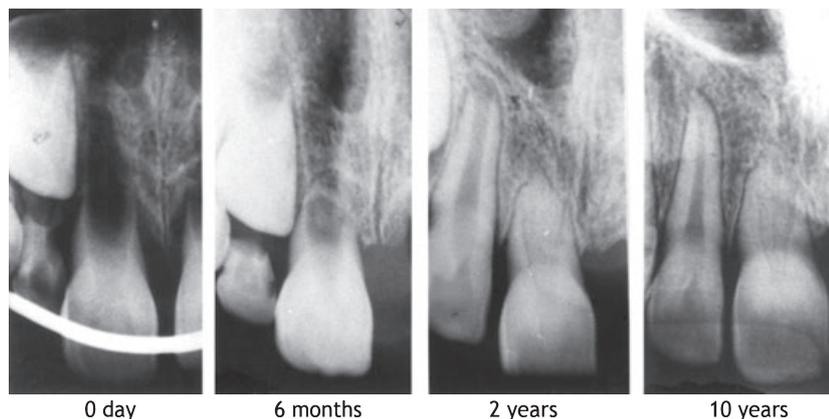


Fig. 3. Ingrowth of bone and cementum and periodontal ligament into the pulp canal after replantation of an avulsed incisor.

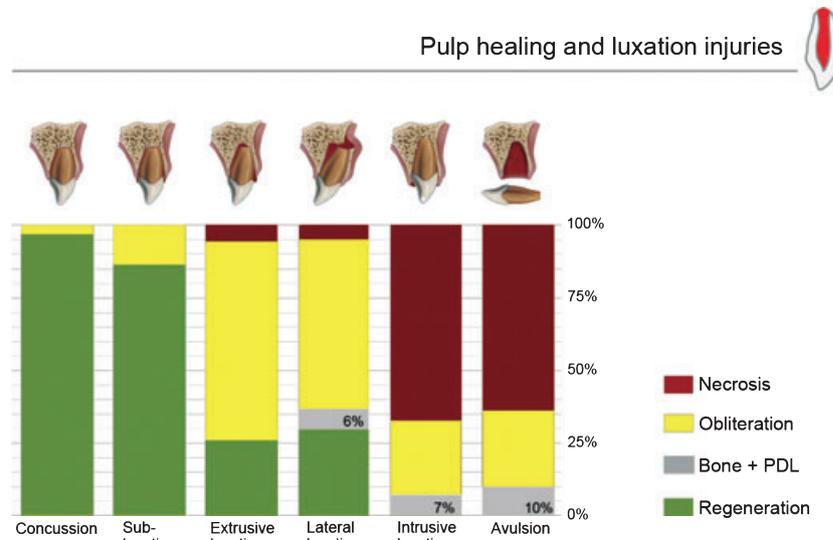


Fig. 4. Frequency of bone and periodontal ligament ingrowth (along with other outcomes) in teeth with incomplete root formation and related to various luxation injuries. From Andreasen, Malmgren & Tsilingaridis (in preparation).

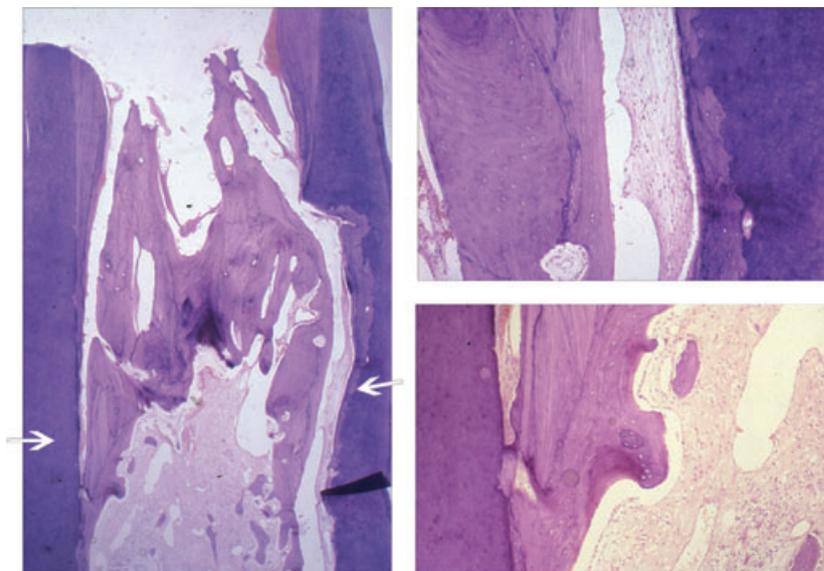


Fig. 5. Internal bone and periodontal ligament has resulted in ankylosis-related resorption whereby the eruption of the incisor was arrested leading to infraposition of the tooth. The arrow indicates the site of fusion (ankylosis) between the bone and the canal wall. From Cvek (30).

the mid-root section, and this indicates that the internal PDL development does not offer the usual PDL protection against resorption (ankylosis) (29, 46). The homeostasis phenomenon possibly includes the presence of Mallasez epithelial islands in the PDL, and these islands are not found in the PDL forming inside the canal (Malmgren, Tsilingaridis & Andreasen, in preparation).

Ingrowth of bone and bone marrow into the pulp space

This type of tissue ingrowth is a rare finding. It has been reported in relation to experimental transplantation of third molars in monkeys (51) and can also be seen after

luxation injuries with displacement (52, 53). A unique variation in this bony invasion of the pulp space is an internal tunneling resorption where 'cutting cones' related to bone remodeling appear as longitudinal resorption channels running parallel to the pulp canal (36) (Fig. 6). This process can be seen from radiographic follow ups to be arrested over time.

Conclusion

As attempts are being made to induce 'regeneration' or revitalization of necrotic pulpal tissue, it may be important to consider what type of tissue one may be able to

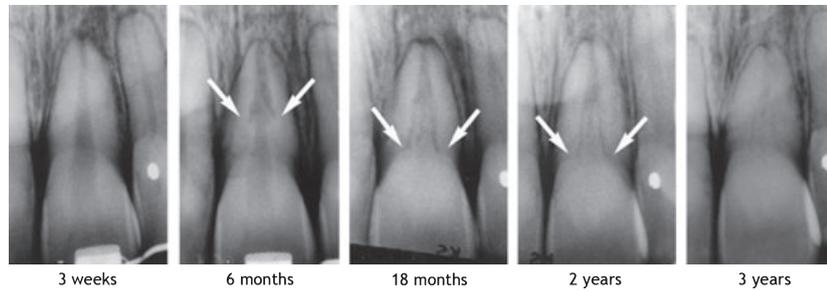


Fig. 6. Internal tunneling resorption parallel to the root canal developed after extrusion of a central maxillary incisor. Continued pulp canal obliteration proceeded irrespective of the tunneling. From Andreasen & Andreasen (36).

produce. This would appear to be a critical question to address during the process of replacing conventional endodontic procedures with a new 'regenerative' approach to treating incompletely developed teeth with pulpal disease.

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