Apexification: review of the literature

Donald R. Morse* / James O'Larnic** / Cemil Yesilsoy***

Five methods for the treatment of teeth with an incompletely formed apex (open apex) and a necrotic pulp are discussed. The methods discussed include the use of (1) a customized cone (blunt-end, rolled cone); (2) a short-fill technique; (3) periapical surgery (with or without a retrograde seal); (4) apexification (apical closure induction); and (5) one-visit apexification. The apexification techniques, which use various formulations of calcium hydroxide to induce closure, are stressed. Based on the review of the literature and clinical experience of the authors, it was concluded that successful treatment of an immature pulpless tooth can partly result from the antibacterial and calcification-inducing action of calcium hydroxide. (Quintessence Int 1990;21:589-598.)

Introduction

Apexification is a method of inducing apical closure through the formation of mineralized tissue in the apical pulp region of a nonvital tooth with an incompletely formed root (open apex). The mineralized tissue can be composed of osteocementum, osteodentin, or bone or some combination of the three. Apical closure can take various forms. It can be a complete or an incomplete hard tissue bridge a few millimeters short of the end of the root. It can be located at the tip of the root, or the bridging can be an irregular mass of calcification traversing the apical one third of the root. In most cases, apical closure takes an irregular and aberrant form. Along with apical closure, root development or lengthening may or may not continue, but whatever the form, root development is usually irregular and aberrant. In contrast, apexogenesis treatment (vital root-end closure) results in regular apical closure and normal-appearing root development.

Currently, there are at least five methods of treating a tooth that has a necrotic pulp and an open apex. These methods are (1) filling the root canal with the large (blunt) end of a gutta-percha cone or customized gutta-percha cones with a sealer; (2) filling the root canal well short of the apex (before the walls have diverged) with gutta-percha and sealer or zinc oxide-eugenol (ZOE) alone; (3) filling the root canal with gutta-percha and sealer as well as possible and then performing periapical surgery with or without a reverse seal; (4) inducing apical closure by the formation of an apical stop (calcium hydroxide [Ca(OH)₂] is generally used) against which a permanent root canal filling can subsequently be inserted; and (5) placing a biologically acceptable substance in the apical portion of the root canal (dentine chips or tricalcium phosphate have been used) thus forming an apical barrier; this is followed by filling the root canal with gutta-percha and sealer. The last procedure has been called one-visit apexification. Each of these techniques will be examined.

Blunt-end or rolled cone (customized cone)

Filling the root canal with the large end of a gutta-percha cone or a customized cone is not advisable because the apical foramen is generally wider than the root canal orifice. This would prevent proper condensation of the gutta-percha, and proper preparation of the canal would weaken the tooth considerably. It would also be difficult to assess the point of root de-
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Development radiographically because root formation in the buccolingual plane is less advanced than it is in the mesiodistal plane.11

Short-fill

Moodnick12 proposed removal of the bulk of the necrotic tissue and filling the root canal short of the apex with gutta-percha. He advocated use of Diakelet® (Premier Dental Products), a compound of beta-ketones and zinc oxide, in place of gutta-percha to enhance healing. However, with an incomplete obturation, microbes can be left remaining within the apical part of the root canal system, and healing may not take place or periapical breakdown may occur later.13

Periapical surgery

The gutta-percha/sealer surgical approach has many drawbacks. Many clinicians do not advocate this method of treatment for one or more of the following reasons:

1. Relative to the already shortened roots, further reduction could result in an inadequate crown-to-root ratio.
2. Surgery could be both physically and psychologically traumatic to the young patient.
3. The young patient is not apt to be cooperative.
4. Surgery would remove the root sheath and prevent the possibility of further root development.
5. The apical walls are thin and could shatter when touched by a rotating bur.
6. The thin walls would make condensation of a retrograde material difficult. This can result in an inadequate seal.
7. The periapical tissue may not adapt to the wide and irregular surface of the amalgam.

However, for cases in which a more conservative approach is not feasible, Dawood and Pitt Ford21 have given evidence that the obturation of the root canal with thermoplasticized gutta-percha/sealer followed by periapical curettage can be clinically successful.

Apical closure induction

Induction of apical closure or an apical stop has become the most widely used approach to treating these teeth. Many materials and methods have been used successfully, but the exact mechanism of action remains a mystery. It has been considered that in the treatment of teeth with a necrotic pulp, the basic aim should be stimulation and preservation of the formative activity of the granulation tissue cells in the apical part of the root canal. This should enhance the formation of a calcified callus in the wide apical opening.22

The use of Ca(OH)2 to induce apical closure was first introduced in 1964 by Kaiser,23 when he proposed that use of Ca(OH)2 mixed with camphorated parachlorophenol (CMCP) would induce the formation of a calcified barrier across the apex. His procedure was popularized in 1966 by Frank,24 who described a step-by-step technique and four types of apical closure. For the procedure to be effective, it has been hypothesized that Ca(OH)2 paste must contact vital tissue, although this has never definitely been proven.24 It has also been shown that the larger the apical opening, the longer the time necessary to induce apical closure. However, no consensus exists on how frequently the dressings have to be changed to induce apexification.24,23,25,26

Heithersay25,27 and others28,29 have induced apical closure using Ca(OH)2; and methylcellulose (Pulpdent, Pulpdent Corp). Pulpdent has the advantages of decreased solubility in tissue fluids and firm physical consistency.27

A different approach with Pulpdent has been used by Senzamici and Tesini.30 In their technique, a master cone is fitted 3 mm from the apex, and, prior to obturation, the apical 3 mm is filled with Pulpdent. Nygaard-Ostby31 suggested laceration of the periapical tissues with a file until bleeding occurs, to result in the further development of the root apex. Zussman32 showed that the vascularity of the apical region facilitates and favors further root development by the root sheath once the tissues are in a healthy state. However, Ham and coworkers33 have not reported much success with the induced blood clot,30 and Citrome and coworkers34 have reported that the blood clot maintained the initial inflammatory state and did not result in hard tissue bridging at the apex.

Rule and Winter35 utilized instrumentation to induce bleeding and believed that this tissue may have not undergone necrosis and could therefore aid in further apical closure and root development. Tornoeck and Smith36 reported that any attempt to retain a residual pulp stump in the apical one third of the root canal results in the formation of a periapical abscess. They also reported that, despite the absence of remedial therapy, continued root growth can occur. The calcific bridge at the apex in some cases appears to be related more to the ingrowth of trabecular bone.
Leiberman and Trowbridge37 and Barker and Mayne38 have reported cases of root-end closure without pulp therapy or endodontic therapy. Israel3 was able to obtain continued apical development after use of biomechanical cleaning alone. Das39 considered that minimal mechanical intervention and removal of infection alone would be sufficient to induce apical closure. Conversely, other studies40-42 have reported that cases in which the root canals were thoroughly cleaned and shaped had a decreased incidence of root formation compared to cases in which the root canals were instrumented less thoroughly. England and Best43 stated that the thorough cleaning of the root canal may be the primary factor responsible for apical closure. They believed, as did Chawla and coworkers,44 that a catalyst paste is unnecessary to induce apical closure. Some investigators45,46 concluded that, although apexification is a natural phenomenon, it must be stimulated by a biologic activator.

Klein and Levy37 and others48,49 have successfully induced apical closure using Ca(OH)2 and Cresatin (Premier Dental Products), a metacresylacetate. Weiss,50 using this mixture as a pulp capping agent, reported more rapid healing with it than with the use of Ca(OH)2 and water.

Cresatin has been shown to have minimal inflammatory potential as a root canal medicament51 and minimal cytotoxicity when compared with CMCP.52 Camphorated parachlorophenol has also been shown to be a highly toxic preparation capable of causing tissue necrosis. However, Dylewski33 saw no evidence of irritation after use of CMCP in the periapical tissues of monkeys.

If CMCP or Cresatin is mixed with Ca(OH)2, a chemical reaction occurs and results in the formation of the calcium-p-chlorophenolate and calcium cresylate salts, and, after 2 weeks, Ca(OH)2 and Cresatin have been observed to form acetic acid.43 These compounds are difficult to remove from root canals.50 It has also been shown that the combined pH of Cresatin and Ca(OH)2 decreases faster than the pH of the combined CMCP and Ca(OH)2.

Calcium hydroxide, when mixed with a number of different substances, has been successful in inducing apical closure.53,54 Since its introduction, Ca(OH)2 has been mixed with CMCP,55 distilled water,55 sterile water,56,57 sterile saline,58 anesthetic solutions (preferably without vasoconstrictors),59 chlorothymonal,60 Cresatin, Cresanol (Premier Dental Products), a mixture of CMCP and Cresatin, Ringer's solution, methylocellose, and iodoform.61 In some formulations, glycerine has been added to improve the consistency, and barium sulfate has been added to make the paste more radiopaque.62 However, Smith and Woods63 suggested that the use of diatrizoate compounds (soluble organic iodine) be used as a substitute for barium sulfate. The diatrizoate compounds are resorbable and will not obscure the apex if the paste is extruded periapically.

Other pastes have been used to induce apical closure, including pastes that contain antibiotics35,64-66 Cooke and Rowbotham66 used an antiseptic paste containing zinc oxide, cresol, clove oil, iodoform, and thymol. Other investigators67,68 consider this apical paste to be a protoplasmic poison that would further irritate the periapical tissues.

When Vojinovic and Srnic39 compared the use of Ca(OH)2 to the use of iodoform Chumsky paste (30 g phenol, 30 g camphor, 110 g absolute alcohol), they found more calcified tissue and a more complete closure with Ca(OH)2. They believed that, although some stimulation of the cells of the granulation tissue is necessary, the paste was more irritating than is necessary.

Other materials that have been used with some success are Calosept (Scania Dental),71 an iodoform-containing paste,72 Hypocal (Elliott Co.),73 a chlorometacin-containing paste,40 and ZOE pastes.74 Bernard75 showed that apical development occurred after sterilization of the periapical tissues followed by filling of the root canals with a calcium oxide-containing paste. Matsumiya and Kitamura76 compared the effect of antibacterial treatment using antiseptic and antibiotics with the effect of physiologic saline before the canals were filled with Ca(OH)2. The comparison was a histopathologic and histobacteriologic examination of the root canals from the teeth of infected dogs. There was no statistically significant difference between the two groups. This can be related to the long-term antibacterial effect of the Ca(OH)2, which has been demonstrated, in vitro, to be bactericidal and antiseptic. According to some authorities, the chance of a successful outcome are lessened if a negative microbiologic culture cannot be obtained.77 The formation of calcified tissue is considered to occur in the absence of microorganisms.77,78 It has been shown that Ca(OH)2 accelerates hard tissue bridging at the apex irrespective of the initially induced inflammatory state.34

A study by England and Best43 found that apical closure occurred more frequently in teeth left open to the oral environment (86.5%) than in those closed to
calcium phosphate (Ca[PO].i) complexes, which would, in turn, serve as a nidus for further calcification. Javellet and coworkers also indicated that the alkalinity is a significant feature in the ability of Ca(OH)₂ to induce hard tissue formation. Other investigators contended that Ca(OH)₂ creates an unfavorable environment for osteoclastic activity or can activate alkaline phosphatase enzymes. The latter have been suggested as playing a role in hard tissue formation. Yesilsoy and coworkers have shown that Ca(OH)₂, by itself and as a component of root canal sealers, can induce calcification even in a soft tissue environment. When preparing the Ca(OH)₂ paste using anesthetic solutions, Stamos and coworkers determined that such a small amount of liquid is used that no appreciable change occurs in the pH. Mitchell and Shankwalker concluded that it is difficult to ascribe any importance to the pH of the material when the osteogenic potential is considered. They rationalized that the use of other materials that have relatively high pH values do not result in consistent hard tissue formation. This is also supported by the investigations of Binnie and Mitchell.

McCormick and coworkers maintained that the reliance on medication alone to accomplish a pH rise in the periapex, as proposed by Van Hassel and Natkin, is unrealistic. They believed that other procedures are of considerable importance in gaining continued apical development. These procedures include (1) adequate preparation of the root canal; (2) removal of necrotic tissue and substrate; (3) reduction of microbes (both in terms of numbers and virulence); and (4) a decrease in the root canal space. Frank concluded that the reduction of contaminants in the root canal and the filling of the root canal space with a temporary resorbable material are more important than which material is used.

Nyborg and other investigators thought that pulpal reaction to Ca(OH)₂ depended on the hydroxyl ion rather than the calcium ion. Nevertheless, in one study, in which magnesium hydroxide (Mg(OH)₂) was used in 14 apexification procedures, the results showed four mild and ten severe inflammatory reactions. Contradictory results were found when Mg(OH)₂ was implanted subdermally in rats. Magnesium hydroxide was found to have less of an inflammatory reaction than has Ca(OH)₂. In one investigation, barium hydroxide was substituted for Ca(OH)₂. Observations from this study included a lack of bridge formation, a severe foreign body reaction, and acute and chronic inflammation with epithelial proliferation.
The calcium ion was also thought to be necessary to decrease capillary leakage and constrict the pre-capillary sphincters. In addition, the calcium ion can also affect the enzyme pyrophosphatase, which is calcium dependent. Pyrophosphate is involved in collagen synthesis and, therefore, stimulation of this enzyme can increase the defense and repair mechanisms.

Nevins and coworkers used a Ca(PO)₄ gel to produce a mineralized scar around the orifices of polyethylene tubes that were placed subcutaneously in rats. When placed in pulpless open-apex teeth in monkeys, the gel resulted in connective tissue ingrowth. Nevins et al. postulated that this could be a step in revitalization of teeth. In other studies, the Nevins group also reported the successful use of collagen Ca(PO)₄ gel. Donlon has shown that calf skin collagen is immunologically neutral. In contrast, Citrome and coworkers found that, in dogs, the collagen Ca(PO)₄ gel inhibited the reparative process of the initial inflammatory lesion, leading to extensive destruction of the periapical tissues. No evidence of apexification was found. Heuer reported that collagen Ca(PO)₄ gel failed to assist in the resolution of instrumentation trauma and inhibited the repair process. Teeth treated with Ca(OH)₂ in the same animals showed an acceleration of the repair process.

Finally, whether or not a complete apical barrier results from apexification techniques is uncertain. Lieberman and Trowbridge have shown that even with radiographic and clinical evidence of a hard tissue barrier, histologic examination shows that this barrier is porous. Nevertheless, for clinical success, it may not be necessary to have an impermeable hard tissue barrier.

**One-visit apexification**

The most recent development in the treatment of teeth with a necrotic pulp and an open apex is to condense nonsurgically a biocompatible material into the apical end of the root canal. The rationale is to establish an apical stop that would then enable the root canal to be filled immediately. This technique has been called a one-visit apexification. However, it really only fulfills one aspect of apexification: the creation of an apical stop. It does not allow for continued root development. Hence, the technique cannot be used for teeth with excessively short roots.

A resorbable ceramic has also been developed. It is a specially prepared form of calcium phosphate that (1) acts as a matrix for the invasion of blastic cells, (2) allows for cellular proliferation and differentiation, and (3) permits deposition of hard tissue. Studies have shown that resorbable ceramic is replaced by bone.

Koenigs and coworkers simulated conditions of an open apex in 24 monkey teeth and packed the apical 3 to 4 mm with calcium phosphate ceramic. At the end of a 24-week period, most of the material had been resorbed and replaced by a mineralized tissue that contained nuclei. The tissue extended 3 to 5 mm into the root canal, and it resembled cementum. The periodontal ligament had regenerated with little, if any, inflammation of the periapical tissues. However, the bridge was not complete, and a small channel, containing connective tissue and blood vessels, was observed on one lateral wall.

Roberts and Brilliant compared apical closure between triCa(PO)₄ (pH = 8.6) and Ca(OH)₂ (pH = 12.0). Both substances are relatively successful. They concluded that the use of a highly alkaline material is unnecessary to induce closure and that particle size might be a factor. TriCa(PO)₄ and Ca(OH)₂ had nearly identical particle sizes (Ca(OH)₂ = 2 to 5 μm; triCa(PO)₄ = 5 to 5 μm).

Coviello and Brilliant compared a one-appointment technique using either Ca(OH)₂ or triCa(PO)₄. Both substances proved successful, but, in contrast to the previously mentioned study, more Ca(OH)₂ was necessary to create the apical stop. This result was probably due to discrepancies in particle size.

Dimashkieh devised a technique using Surgicel (Ethicon Ltd) along with amalgam. Surgicel is an oxidized regeneration cellulose that is nonirritating and resorbable. After preparation of the root canal, the Surgicel was inserted through the access opening and packed apically. This was followed by insertion of the amalgam in the same fashion. Hence, the Surgicel was used as a base and/or matrix.

Rossmeisl and coworkers used freeze-dried cortical bone and freeze-dried dentin to create apical plugs. They found that both materials were biocompatible with periapical tissues. The freeze-drying procedure appears to inactivate the histocompatible antigens.

The use of dentinal shavings as a root canal filling material was first described by Gollmer in 1937. Tronstad has found dentinal chips to be well tolerated by periapical tissues. Others have found that the use of dentinal chips increases the formation of osteocementum in the periax.
**Table 1** Summary of techniques for treatment of nonvital teeth that have an open apex

<table>
<thead>
<tr>
<th>Technique</th>
<th>Root-end closure</th>
<th>Histologic response</th>
<th>Appointments</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated</td>
<td>Yes, but only case reports</td>
<td>Questionable</td>
<td>None</td>
<td>Poor</td>
</tr>
<tr>
<td>Instrumentation alone</td>
<td>Yes, but may be decreased amount</td>
<td>Questionable</td>
<td>1-2</td>
<td>Questionable</td>
</tr>
<tr>
<td>Customized cone</td>
<td>No</td>
<td>Unfavorable</td>
<td>2-3</td>
<td>Poor</td>
</tr>
<tr>
<td>Short fill</td>
<td>Yes, but only case reports</td>
<td>Questionable</td>
<td>2-3</td>
<td>Poor</td>
</tr>
<tr>
<td>Periapical surgery</td>
<td>No</td>
<td>Unfavorable</td>
<td>1</td>
<td>Fair</td>
</tr>
</tbody>
</table>

**Apexification**

- Calcium hydroxide
- Magnesium hydroxide
- Barium hydroxide
- Zinc oxide
- Calcium oxide
- Calcium phosphate collagen gel
- Tricalcium phosphate
- Other pastes

<table>
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<th>Appointments</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium hydroxide</td>
<td>Yes</td>
<td>Favorable</td>
<td>6-7</td>
<td>Generally good</td>
</tr>
<tr>
<td>Magnesium hydroxide</td>
<td>No</td>
<td>Questionable</td>
<td>6-7</td>
<td>Poor</td>
</tr>
<tr>
<td>Barium hydroxide</td>
<td>No</td>
<td>Unfavorable</td>
<td>6-7</td>
<td>Poor</td>
</tr>
<tr>
<td>Zinc oxide</td>
<td>Questionable</td>
<td>Unfavorable</td>
<td>6-7</td>
<td>Poor</td>
</tr>
<tr>
<td>Calcium oxide</td>
<td>Yes</td>
<td>Questionable</td>
<td>6-7</td>
<td>Fair</td>
</tr>
<tr>
<td>Calcium phosphate collagen gel</td>
<td>Questionable</td>
<td>Questionable</td>
<td>6-7</td>
<td>Questionable</td>
</tr>
<tr>
<td>Tricalcium phosphate</td>
<td>Yes</td>
<td>Favorable</td>
<td>6-7</td>
<td>Generally good</td>
</tr>
<tr>
<td>Other pastes</td>
<td>Questionable</td>
<td>Questionable</td>
<td>6-7</td>
<td>Questionable</td>
</tr>
</tbody>
</table>

**One-visit apexification**

- Resorbable ceramic
- Tricalcium phosphate
- Calcium hydroxide
- Surgicel/amalgam
- Freeze-dried bone or or dentin

<table>
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<th>Prognosis</th>
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<tr>
<td>Resorbable ceramic</td>
<td>No</td>
<td>Favorable</td>
<td>1</td>
<td>Fair</td>
</tr>
<tr>
<td>Tricalcium phosphate</td>
<td>No</td>
<td>Favorable</td>
<td>1</td>
<td>Fair</td>
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<tr>
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</table>

Weisenseel and associates compared apical seals of root canals mechanically prepared to simulate open apexes. The root canals were then filled with either gutta-percha and Tubli-seal (Kerr/Sybron Corp) alone, or an initial placement of a 2-mm apical plug of Ca(OH)₂ before the gutta-percha/sealer combination. The results indicated that the root canals with apical plugs (Ca(OH)₂) demonstrated significantly less leakage than did those without the plugs.

**Discussion**

Five methods are primarily used to manage teeth with an open apex and a necrotic pulp: (1) use of the blunt end of a gutta-percha cone or rolled gutta-percha cones; (2) obturation of the root canal short of the apex; (3) performance of periapical surgery with or without a reverse amalgam seal; (4) use of an apexification procedure to create an apical stop; and (5)
use of a one-visit apexification procedure by condensing a biologically acceptable material in the apex followed by obturation of the rest of the root canal with gutta-percha/sealer (Table 1).

The most frequently used procedure appears to be apexification with Ca(OH)$_2$. Its relatively good success has been attributed to one or more of the following properties: (1) the pH; (2) the calcium ion; (3) the hydroxyl ion; and (4) the antibacterial effect. However, the property that actually promotes the mechanism for calcif;e bridge formation is not known. Before a wound can heal properly, the bacteria in the area must be removed, inactivated, or greatly reduced in number. Although Ca(OH)$_2$ possesses antibacterial properties, apexification has also been successful without the use of this medicament. The common aspects of all apexification procedures are debridement, cleaning, and reduction of the root canal space with a material, thus leading to a favorable periapical environment.\(^{18,19}\) Once the infection is eliminated and the periapical tissues reorganize, it is then possible for calcific development to take place.\(^{18}\) Frank\(^{19}\) has stated that Ca(OH)$_2$ paste is often used as a temporary paste filling because of its availability and its comparative ease of removal rather than because of any unique effect.

With the current popularity of single-visit endodontics,\(^{21}\) there has emerged a single-visit apexification as the result of the formation of an operator-made apical barrier. The successful performance of this one-visit procedure benefits both the patient and the practitioner because of the reduced amount of office time required. The problem of patient compliance is also reduced, and this can eliminate the problems that can arise with extended treatments. In addition, it appears that with multiple visits, the reopening of the root canal, and its recleaning, disturbs the process of apexification.\(^{42,71}\) However, there are reports of conflicting results with one-visit apexification procedures.\(^{104-108}\) This technique has been performed on dogs, monkeys, and humans and in cases of (1) intact, healthy teeth; (2) experimentally infected teeth; (3) teeth with a naturally wide open apex; and (4) teeth with a simulated open apex. To evaluate one-visit apexification properly, a standardized method has to be devised.

Conclusions

The eventual successful outcome in the treatment of an immature pulpless tooth can partly result from the antibacterial and calcification-inducing action of calcium hydroxide. Which Ca(OH)$_2$ preparation is best is unknown. Suggestions include Ca(OH)$_2$ with distilled water, sterile saline, local anesthetic solution, Cresatin, CMCP, methylcellulose, resins, and other substances. However, there is no evidence of the superiority of any combination over plain Ca(OH)$_2$. In addition, the major factors appear to be the debridement of the root canal and the reduction of the root canal space with a space-occupying material. The latter two aspects appear to allow the body to reorganize and repair the periapical tissues.

To evaluate one-visit apexification further, a standardized method or model must be developed to compare the various materials being advocated.

References


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3. Establishing the Foundations
4. Calculation of Oral Care Needs Personnel
5. Examples of Calculations
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