Abstract
This article will describe requirements for case selection and review the procedures for apexogenesis and apexification in immature permanent teeth. Nonclinical and clinical data will be presented to support the recommendations, and outcomes will be presented from clinical studies. The dental pulp is an ectomesenchymally derived connective tissue with certain unique properties such as being encased in hard tissues, which limits its collateral circulation. The pulp provides a matrix for binding of its cells and provides support allowing communication between the cells. In addition to immune cells, the dental pulp contains odontoblasts, which are specialized cells capable of producing dentin. In the absence of a vital pulp, dentin deposition is arrested. When an immature tooth is affected by caries or trauma, the pulp requires proper management according to the degree of inflammation and its vitality. Maintenance of pulp vitality will allow continued root development along the entire root length. If the pulp is irreversibly inflamed or necrotic, root-end closure procedures are required when the apex has not fully formed. (J Endod 2013;39:S26–S29)

Key Words
Apexification, apexogenesis, immature permanent teeth, treatment

Role of the Dental Pulp in Tooth Development
The dental pulp contains immune cells that allow it to mount a response against offending irritants. The pulp also contains odontoblasts, which are specialized to form dentin. In the absence of a vital pulp, the tooth structure is susceptible to infection, and dentin deposition is arrested. Maintenance of pulp vitality is imperative in an immature permanent tooth to allow continued root development. The pulp tissue is removed when pathologically inflamed or necrotic.

Although studies are underway to develop materials and techniques for pulp regeneration procedures, the purpose of this review is to provide an overview of apexogenesis and apexification in immature permanent teeth with pulpal pathosis.

Apexogenesis or Apexification
Proper assessment of the affected tooth is critical in determining an accurate diagnosis and prescribing the appropriate treatment plan. Assessment of pulp vitality will aid in determining the proper treatment option. If vital and not irreversibly inflamed, maintenance of its vitality will allow natural continued root development. Figure 1 presents a flow chart to facilitate the decision-making process when treating permanent teeth with incomplete root development.

Assessment of the tooth in question is made by using radiographic evaluation to determine the maturity of the developing root and clinical evaluation that is based on history and clinical testing. Obviously immature teeth are frequently associated with child patients. Pulp testing in children is a complex procedure and subjective in nature.

Maintenance of pulp vitality by using apexogenesis will allow continued root development along the entire root length. Depending on the extent of inflammation, pulp capping, shallow pulpotomy, or conventional pulpotomy may be indicated. The dental pulp in young patients is more cellular and able to recover from injuries. Cvek et al (1) demonstrated that in teeth with complex crown fractures, the exposed pulp maintained its vitality for up to 7 days. In these teeth, only the most superficial 2 mm of the pulp is inflamed and requires removal.

If pulpal necrosis occurs in immature teeth, an alternative treatment approach must be used because of the presence of an open apex (2). The young pulpless tooth frequently has thin, fragile walls, which makes it difficult to adequately clean and to obtain the necessary apical seal (2). Traditionally, the approach has been to use calcium hydroxide (CH) to induce apexification after disinfection of the root canals in the conventional manner (3). Completion of endodontic therapy was typically delayed until completion of root-end closure through apexification. Apexification is defined as “a method of inducing a calcified barrier in a root with an open apex or the continued apical development of an incompletely formed root in teeth with necrotic pulp” (4).

The disadvantages of traditional, long-term CH therapy include variability in treatment time, unpredictability of formation of an apical seal, difficulty in following up patients, and delayed treatment. An alternative to CH therapy is placement of an apical plug. Several investigators have demonstrated the use of dentin apical plugs in nonsurgical root canal therapy of mature teeth (5–9). Mineral trioxide aggregate (MTA) is a material that may be best suited as an apical plug. In 1999, Shabahang et al (10) showed consistent barrier formation when MTA was used as an apical plug in an in vivo dog model with open apices. Several studies have confirmed successful clinical outcomes including healing of existing periapical lesions in majority of immature teeth that were treated with an MTA apical plug (11, 12).
The advantages of using an apical plug include requirement for fewer appointments to complete the treatment, more predictable apical barrier formation, and reduced need for patient follow-up appointments. The disadvantage of this technique is that, similarly to CH therapy, it only addresses the apical opening and does not account for complete root development along the entire root length. Regardless of the technique used, a critical step in treatment of pulpless teeth with open apices is proper debridement and disinfection of the canal space.

**Disinfection Protocols**

Immature permanent teeth pose special challenges during endodontic procedures not only because of the wide-open root apex but also because of the thin dentin walls. Therefore, debridement is completed primarily by chemical means to remove any remaining pulp tissues and for disinfection. Furthermore, an accurate determination of root length is required to ensure complete canal debridement and to confine treatment materials to the canal space to avoid damaging the very valuable remnants of the Hertwig epithelial root sheath. Generally, electronic apex locators are not accurate in teeth with wide-open apices (13). Radiographic root determination is the best means to obtain accurate root length measurement.

Sodium hypochlorite (NaOCl) and CH have excellent tissue-dissolving properties as well as antimicrobial efficacy (14–18). Whereas NaOCl exerts its effect during the course of the procedure, CH requires additional exposure time. A 1-week obturation of the canal space with CH will allow disinfection along with dissolution and removal of pulpal remnants (19). Despite its convenient availability, several investigators have reported shortcomings with respect to NaOCl’s ability to completely disinfect the root canal space (20–22).

Long-term exposure to CH may also have detrimental effects on dentin. Studies have shown that long-term CH therapy that would expose root dentin to CH for periods exceeding 1 month results in structural changes in the dentin, with higher susceptibility to root fracture (23, 24).

Use of antibiotics has also been documented during the past years and is regaining popularity in recent years. In 1980, Das (25) reported successful apexification of a tooth after root canal debridement and intracanal antibiotic therapy with an oxytetracycline HCl ointment. In 2003, Torabinejad and his group published a series of reports to demonstrate the advantages of a mixture of doxycycline, citric acid, and detergent (BioPure MTAD; DENTSPLY Tulsa Dental Specialties, Tulsa, OK) over NaOCl and other commonly used root canal irrigants (26, 27). MTAD is effective as a final rinse before obturation to disinfect the root canal system and to remove the smear layer. In 2001, Iwaya et al (28) published a case that demonstrated the effectiveness of a double antibiotic paste to disinfect a premolar with a necrotic pulp and a large periapical radiolucent lesion. Three years later, Banchs and Trope (29) published a similar case. In this case report and subsequent studies, Trope’s group recommended a mixture of metronidazole, ciprofloxacin, and minocycline. In *in vitro* studies this antibiotic combination has demonstrated the potential to disinfect the root canal system (30).

**Treatment Outcomes**

Nonclinical and clinical studies have reported good results with a variety of techniques. The most significant shortcoming of long-term CH therapy is the length of time required to complete treatment and frequent challenges in following up with patients over time. A root fracture at the cervical region is a common cause of failure in these cases. Thin dentin at the cervical region and changes in the dentin structure resulting from long exposure times to CH are the causative factors. Table 1 summarizes the outcome results from several studies.

Depending on the study, the speed of barrier formation by using CH therapy varies from 3 to 24 months (2, 31). The suggested time to change the CH in the canal varies from once every 3 months, once every 6–8 months, or not at all (31–33).

Torneck and Smith (34) have indicated that there may be incomplete bridging of the apex, even though a two-dimensional radiograph may give the appearance of complete bridge formation. Periradicular inflammation may persist around the apices of many teeth because of the presence of necrotic tissue in the irregularities of the apical bridge. Therefore, the presence of a radiographically and clinically closed apex is not necessarily indicative of a normal periodontium (35).

Another major drawback of the apexification protocol that uses CH is the effect that a long-term application of CH has on the structural integrity of the root dentin. Several studies have demonstrated that with longer exposures of dentin to CH, its ability to resist fracture is significantly decreased (23, 36).

In a systematic review and meta-analysis comparing the outcomes of CH apexification and MTA apical plug, the authors concluded that the clinical success of both procedures was the same (37). On the basis of the combined data of the 2 studies, the difference in clinical success between the 2 treatment regimens was not statistically significant.

Overall, the results of several studies show that MTA plugs are effective in treating immature permanent teeth with necrotic pulps. The advantages of apexification that uses an MTA plug are reduced treatment time and a more predictable barrier formation. The shortcoming similar to CH therapy, is that placement of an apical plug does not account for continued root development along the entire root length.

Complete root development requires a viable pulp containing cells that can differentiate into dentin-producing odontoblasts. For this, ongoing studies are aiming to identify procedures and materials that allow pulp regeneration. The dental pulp is complex with a variety of cells, nerves, and blood vessels. To regenerate this organelle, it is important to keep in mind the required prerequisites, including cells that are capable of differentiating into pulp cells, the proper signal that is required for the differentiation, and an appropriate scaffold that is suitable for guiding regeneration of the desired tissues, while keeping out the faster growing osseous tissues.

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**Figure 1.** Case selection for treatment of permanent teeth with incomplete root development.
### TABLE 1. Outcomes of Clinical Studies with CH Therapy and MTA Apical Plug

<table>
<thead>
<tr>
<th>Technique/material</th>
<th>Investigator(s)</th>
<th>No. of cases</th>
<th>Observation</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH therapy</td>
<td>Heithersay, 1970</td>
<td>21</td>
<td>14–75 months</td>
<td>Apical canal seen radiographically, but no apical barrier clinically</td>
</tr>
<tr>
<td>CH therapy</td>
<td>Ghose et al, 1987</td>
<td>43</td>
<td>3–10 months</td>
<td>49 of 51 developed an apical barrier</td>
</tr>
<tr>
<td>CH therapy</td>
<td>Morfis and Siskos, 1991</td>
<td>34</td>
<td></td>
<td>Continued root development in 6 cases, continued root development and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>bridge formation in 3 cases, bridge formation in 21 cases, and in</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4 cases no root-end closure</td>
</tr>
<tr>
<td>CH therapy</td>
<td>Lee et al, 2010</td>
<td>22</td>
<td>10–14 weeks</td>
<td>Apical closure in necrotic cases with or without lesion</td>
</tr>
<tr>
<td>CH therapy</td>
<td>Walia et al, 2000</td>
<td>15</td>
<td></td>
<td>100% apical closure with porous barrier. Older children with narrow</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>apex had shorter time; teeth without periapical infection showed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>faster results.</td>
</tr>
<tr>
<td>CH therapy</td>
<td>Dominguez Reyes et al, 2005</td>
<td>26</td>
<td>Average time 12.19 months</td>
<td>Cementoid tissue (85.72%) or osseous tissue (14.28%)</td>
</tr>
<tr>
<td>CH therapy</td>
<td>Mendoza et al, 2010</td>
<td>28</td>
<td>3.24–13.96 months (mean 8.6 months)</td>
<td>Periapical lesions resolved in 4.6 ± 1.5 months for MTA group and in 4.4 ± 1.3 months for CH group. Total treatment was completed in 0.75 ± 0.5 months for MTA group and 7 ± 2.5 months for CH group.</td>
</tr>
<tr>
<td>Comparison of MTA plug with CH therapy</td>
<td>El-Meligy and Avery, 2006</td>
<td>15</td>
<td>12 months</td>
<td>2 of CH teeth had become reinfected, but all teeth treated with MTA plug remained successful</td>
</tr>
<tr>
<td>Comparison of MTA plug with CH therapy</td>
<td>Pradhan et al, 2006</td>
<td>20</td>
<td>8 months</td>
<td>Periapical lesions resolved in 4.6 ± 1.5 months for MTA group and in 4.4 ± 1.3 months for CH group. Total treatment was completed in 0.75 ± 0.5 months for MTA group and 7 ± 2.5 months for CH group.</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Pace et al, 2007</td>
<td>11</td>
<td>2 years</td>
<td>10 of 11 cases healed, and remaining case considered incomplete healing</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Erdem and Sepet, 2008</td>
<td>5</td>
<td>2 years</td>
<td>4 of 5 teeth healed; 1 case in MTA was extruded</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Sarris et al, 2008</td>
<td>17</td>
<td>11.7 years</td>
<td>94.1% clinical success, 76.5% radiographic success; 17.6% uncertain</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Holden et al, 2008</td>
<td>20</td>
<td>12–44 months</td>
<td>Healing rate was 93.75%</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Nayar et al, 2009</td>
<td>38</td>
<td>12 months</td>
<td>All teeth were clinically and radiographically successful</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Annamalai and Mungara, 2010</td>
<td>30</td>
<td>12 months</td>
<td>100% success clinically and radiographically</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Moore et al, 2011</td>
<td>22</td>
<td>Mean follow-up time 23.4 months</td>
<td>Clinical and radiographic success rate of 95.5%; discoloration in 22.7% of teeth</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Simon et al, 2007</td>
<td>43</td>
<td>12 months</td>
<td>81% healed</td>
</tr>
<tr>
<td>MTA plug</td>
<td>Witherspoon et al, 2008</td>
<td>78</td>
<td>Mean recall time was 19.4 months</td>
<td>93.5% of teeth treated in 1 visit healed, and 90.5% of teeth treated in 2 visits healed</td>
</tr>
</tbody>
</table>

A PubMed search was conducted in August 2012 to identify citations with CH, MTA, apical plug, outcomes, and clinical studies.
Acknowledgments

The author denies any conflicts of interest related to this study.

References