Mineral Trioxide Aggregate: A Comprehensive Literature Review—Part III: Clinical Applications, Drawbacks, and Mechanism of Action

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Abstract

Introduction: Mineral trioxide aggregate (MTA) has been recommended for various uses in endodontics. Two previous publications provided a comprehensive list of articles from November 1993–September 2009 regarding the chemical and physical properties, sealing ability, antibacterial activity, leakage, and biocompatibility of MTA. The purpose of Part III of this literature review is to present a comprehensive list of articles regarding animal studies, clinical applications, drawbacks, and mechanism of action of MTA. **Methods:** A review of the literature was performed by using electronic and hand-searching methods for the clinical applications of MTA in experimental animals and humans as well as its drawbacks and mechanism of action from November 1993–September 2009. **Results:** MTA is a promising material for root-end filling, perforation repair, vital pulp therapy, and apical barrier formation for teeth with necrotic pulps and open apexes. Despite the presence of numerous case reports and case series regarding these applications, there are few designed research studies regarding clinical applications of this material. MTA has some known drawbacks such as a long setting time, high cost, and potential of discoloration. Hydroxyapatite crystals form over MTA when it comes in contact with tissue synthetic fluid. This can act as a nidus for the formation of calcified structures after the use of this material in endodontic treatments. **Conclusions:** On the basis of available information, it appears that MTA is the material of choice for some clinical applications. More clinical studies are needed to confirm its efficacy compared with other materials. *(J Endod 2010;36:400–413)*

Key Words

Apical plug, clinical application, drawbacks, mechanism of action, MTA, perforation, pulp capping, pulpotomy, root-end filling, vital pulp therapy

An ideal endodontic repair material should seal the pathways of communication between the root canal system and its surrounding tissues. In addition, it should be nontoxic, noncarcinogenic, nongenotoxic, biocompatible, insoluble in tissue fluids, and dimensionally stable. Because existing materials did not have these "ideal" characteristics, mineral trioxide aggregate (MTA) was developed and recommended for pulp capping, pulpotomy, apical barrier formation in teeth with necrotic pulps and open apexes, repair of root perforations, root-end filling, and root canal filling (1, 2). As recommended by the American Association of Endodontists, the use of a new material and/or method of treatment should be based on laboratory, biologic, and clinical studies (3). Following these steps systematically paves the way for clinical use of a material in experimental animals and then in patients. Two previous publications provided a comprehensive list of articles from November 1993–September 2009 regarding the chemical and physical properties, sealing ability, antibacterial activity, leakage, and biocompatibility of MTA (4, 5). On the basis of the results of these publications, it appears that MTA is a suitable repair material for various endodontic uses. The purpose of this review is to present a comprehensive list of articles regarding animal studies, clinical applications, drawbacks, and mechanism of action of MTA.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for this literature review were identical to those used for Parts I and II of the review (4, 5).

Search Methodology

An electronic search was conducted in the PubMed and Cochrane databases with appropriate MeSH headings and key words related to the animal studies, clinical applications, drawbacks, and mechanism of action of MTA. The hand-searching methodology in this literature review was identical to that used for Parts I and II of the review (4, 5).

Animal Studies

Vital Pulp Therapy

Primary Teeth. In a study on the primary teeth of pigs, Shayegan et al (6) compared white MTA (WMTA) with Dycal, beta-tricalcium phosphate cement, and white Portland cement (WPC) as a pulp capping agent. Their findings showed no significant differences in pulp response between any of the materials.

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Permanent Teeth

Direct Pulp Capping—The formation, quality, and thickness of a calcified bridge, presence of inflammatory cells, and preservation of the pulp are considered evaluation criteria after vital pulp therapy in the majority of the investigations on animal teeth (7–16).

Histologic Studies

Most direct pulp capping investigations have compared MTA with calcium hydroxide (CH) (7, 8, 10, 12, 13, 16). Two studies found the presence of a calcified bridge in many pulp specimens capped with MTA after 1 week (11, 17), whereas several other studies demonstrated calcified bridge formation after 2 weeks in all or most specimens (9, 11, 18). Pitt Ford et al (7) compared CH and MTA as pulp capping agents on monkeys' teeth. Their results showed that the majority of pulps that were capped with MTA were free of inflammation, and all of them showed calcified bridge formation after 5 months. In contrast, the pulp of teeth that were capped with CH showed presence of inflammation and significantly less calcified bridge formation.

In an investigation on dogs' teeth, Faraco et al (8) used MTA or Dycal as pulp capping agents and reported tubular hard tissue formation with no pulp inflammation beneath any MTA sample. In contrast, the majority of Dycal-capped pulps showed presence of inflammation, and only one third of the specimens exhibited calcified bridge formation. On the basis of these results, the researchers concluded that pulp capping with MTA produces significantly better results than with Dycal. In a study with dogs' teeth, Tziafas et al (9) showed osteodentin structure 2 weeks after pulp capping with MTA. They reported that bridge formation occurs under MTA in 2 stages. During the first 2 weeks, osteodentin matrix formation takes place, whereas after 3 weeks, a complete layer of reparative dentin is formed at the capping site.

Dominguez et al (10) used light-cured CH, MTA, and acid-etched dentin bonding (AEDB) as pulp capping agents in dogs' teeth. Statistical analysis of the data in this study revealed no significant difference between MTA-treated pulps and sound, intact control teeth. Significantly more pulpal inflammation was observed in pulps treated with CH or AEDB than in control teeth. The authors concluded that MTA is a considerably better material than CH or AEDB in maintaining the integrity of the pulp.

In a study on rats' maxillary molars, Andelin et al (18) compared bone morphogenetic protein-7 (BMP-7) and MTA as pulp capping agents. The specimens were immunohistochemically stained for identification of dentin sialoprotein (DSP) staining as a marker for functional odontoblasts. After 2 weeks, all MTA-capped teeth showed hard tissue that resembled tertiary dentin and were significantly more positive for DSP in comparison with BMP-7 specimens. The majority of the teeth that were capped with BMP-7 showed formation of bone-like hard tissue at the site of pulp capping, but MTA-capped pulps showed significantly more complete dentin bridge formation.

The first animal study in which WMTA was used as a pulp capping material confirmed its ability to produce a dentin bridge in dogs' teeth (14). In a later investigation, Parirokh et al (11) compared WMTA with gray MTA (GMTA) as pulp capping agents on dogs' teeth. They reported calcified bridge formation in some specimens after 1 week, whereas all of the WMTA and most of the GMTA specimens showed calcified bridge formation after 2 weeks. These authors reported the presence of mild inflammation at the junction of pulp and pulp capping materials that was absent after 2 weeks. No appreciable differences were observed between WMTA and GMTA as pulp capping agents in terms of inflammation and calcified bridge formation.

Briso et al (12) compared the biologic responses of pulp tissue to CH and MTA, confirming the superiority of MTA as a pulp capping material in terms of hard tissue bridge formation and prevention of pulpal infection. Recently, Kuratate et al (17) analyzed the reparative process of exposed rat dental pulps capped with WMTA by examining the deposition of osteodentin, cell proliferation, and the appearance of nestin immunoreactive odontoblast-like cells at the exposure site. Their findings indicated that most proliferative cells are formed beneath the exposure area around pulpal blood vessels. They reported a thin necrotic layer with a few scattered inflammatory cells beneath the capping material after 1 day. In their study, calcified bridge formation was observed 7 days after pulp capping. Another recent study with maxillary molars of mice reported the presence of a calcified bridge in all specimens 5 weeks after capping with GMTA (15).

Hasheminia et al (16) treated pulp exposures with laser radiation followed by pulp capping with MTA and compared these samples with those treated by Dycal and MTA alone. Although their results showed no significant differences between the groups, the authors concluded that a combination of laser and MTA produced better healing in terms of calcified bridge formation, presence of necrosis, and type and intensity of inflammation.

Some systemic disorders might adversely affect the repair potential of pulp tissue. In an animal study, mechanical dental pulp exposure in intentionally induced hyperglycemic rats showed more inflammation and demonstrated a lower rate of dentin bridge formation compared with normal rats, despite using MTA as the capping material (19). Most animal studies comparing MTA with other pulp capping agents showed more favorable results with MTA (7, 8, 10, 12, 13). None of the studies that compared WMTA and GMTA showed significant difference in pulp response to either of the materials in terms of calcified bridge formation, inflammatory reaction, and necrosis.

Electron Microscope Observations

In a transmission scanning electron microscope (TEM) and scanning electron microscope (SEM) investigation on dogs' teeth, Tziafas et al (9) evaluated pulpal reaction to MTA as a pulp capping material. They reported a crystalline structure along the pulp-MTA interface 1 week after pulp capping. Another investigation showed that the amount of minerals and organic components in the bridge formed beneath the capping material is different for various pulp capping materials (10).

In an investigation on dogs' teeth, Asgary et al (20) used WMTA as a pulp capping material and confirmed the results of the previous study by Tziafas et al (9). In a recent study on murine teeth, Simon et al (15) used MTA as a pulp capping material. Using an energy-dispersive x-ray spectrometer system, the investigators reported that the reparative dentin beneath MTA exhibits less calcium than previously formed orthodentin. These electron microscope observations showed that the calcified bridge at the capping area is mainly composed of calcium and phosphorous, whereas MTA itself is composed of mainly calcium and silica.

Pulpotomy

Primary Teeth. In a histologic study, Shayegan et al (21) compared 5 pulpotomy agents on the primary teeth of pigs for pulp inflammatory response, calcified bridge formation, and preservation of normal dental pulp. Formocresol (FC) and ferric sulfate proved to be irritating to the pulp. In contrast, no significant differences were noted between beta-tricalcium sulfate, WMTA, and WPC, with all 3 materials illustrating biocompatibility.

Permanent Teeth

Histologic Observation—Several investigations in animal models (rats and canines) have compared MTA with PC, light-cured CH, powder CH mixed with saline, AEDB, FC, bioactive glass, and ferric

sulfate (10, 22–25). Holland et al (22) compared PC with MTA as pulpotomy materials on dogs' teeth and reported similar histologic results for both materials. Dominguez et al (10) used light-cured CH, MTA, and AEDB as pulpotomy agents in dogs' teeth. Statistical analysis of the results established that pulpal inflammation in both CH and AEDB-treated samples were not significantly different than the control teeth 50 days after pulp capping, whereas both materials showed significant differences with control teeth after 150 days. In contrast, MTA-treated samples displayed no significant difference in terms of pulpal inflammation compared with the control samples in both 50-day and 150-day observation periods.

Salako et al (25) compared FC, bioactive glass, ferric sulfate, and MTA as pulpotomy material in maxillary molars in rats. MTA specimens showed complete dentin bridge formation 4 weeks after pulp capping. They reported that among all of the materials that were used in their study, MTA proved to be the ideal pulpotomy agent in terms of dentin bridge formation and preserving normal pulpal architecture.

Menezes et al (23) reported hard tissue formation without pulp necrosis in dogs' teeth after pulp capping with MTA after 120 days. In a histologic study, de Souza Costa et al (24) compared CH and GMTA as pulpotomy agents in dogs' teeth. They reported that CH-capped teeth demonstrate a greater loss of healthy pulp tissue compared with GMTA. They attributed this finding to the higher initial pH value of the CH and the better sealing ability of MTA. The authors found a lack of hard barrier formation and signs of discrete or moderate inflammatory responses in the pulp tissue of the specimens that revealed bacteria in the cavity wall or inside the pulp space.

An investigation on premolar of monkey teeth reported the importance of pretreatment of contaminated pulp exposures with antibacterial agents before using MTA as a pulpotomy agent. In this experiment, cotton pellets moistened with Otic suspensions (Otosporin Otic solution; Wellcome, São Paulo, Brazil) were placed over the contaminated pulp exposures for 5 minutes before MTA was placed. The pulpal tissue treated with Otic suspensions demonstrated significantly less inflammation than the FC and control groups (26).

On the basis of the above data, it appears that favorable results are obtained when MTA is used as a pulpotomy agent in primary and permanent teeth.

Electron Microscope Observations—SEM observations and x-ray analysis presented in a study by Dominguez et al (10) determined that the hard tissue that forms under light-cured CH, MTA, and AEDB is slightly different in both organic and mineral elements. Their chemical assessment showed that the content of both phosphorous and calcium in the hard tissue formed under the capping materials is higher than the levels found in the control samples. A recent investigation comparing ProRoot MTA with CH showed that the calcified barrier in the former group is significantly more tubular than in the latter group (27).

Root-end Filling

Many investigations have compared MTA as a root-end filling material with other currently used materials (28–38). Several investigations concerned infected root canals and induced periapical lesions before filling root-end preparations with MTA (29, 33–35, 37), whereas in others, periapical surgeries were performed after root canal therapy in sound, intact teeth (28, 30, 32).

In the first investigation on MTA as a root-end filling material in dogs, Torabinejad et al (29) showed that the material promotes cementum formation in 23% of specimens 2–5 weeks after periapical surgery. More than 80% of the root-end cavities filled with MTA showed cementum deposition 10–18 weeks after surgery. In contrast, none of the root-end cavities filled with amalgam showed cementum deposition. Another investigation on monkeys established MTA's superiority (less inflammation and cementum formation at 5 months) over amalgam as a root-end filling material (30). In an investigation on dogs' teeth, Regan et al (32) compared Diaket and MTA as root-end filling materials and reported no significant difference between these materials in terms of regeneration of the periradicular tissues 60 days after surgery. Baek et al (34) compared Super EBA, amalgam, and MTA in dogs' teeth as root-end filling materials. MTA showed the most favorable results in terms of degree of polymorphonuclear infiltration, bone maturation, and cementum formation.

In contrast to these histologic findings, Bernabe et al (37) reported no significant difference among MTA, intermediate restorative material (IRM), and Super EBA as root-end filling materials in pulpless teeth 180 days after surgery. They determined that zinc oxide–eugenol (ZOE) had a significantly more negative influence on the apical healing than other test materials, and only MTA stimulated hard tissue deposition in direct contact with the root-end filling material. The same authors again assessed the histologic response of GMTA or ZOE as root-end filling materials in dogs' teeth without root canal fillings and coronal restorations, demonstrating less periapical inflammation and more cementum formation in specimens treated with MTA than ZOE (35).

A recent dog study assessed the healing of periapical tissues of contaminated teeth by using IRM, Geristore, and MTA. Geristore showed the least favorable healing in the histologic evaluation; no statistical difference was noted between MTA and IRM (38).

On the basis of these studies, it appears that MTA produces favorable results when it is used as a root-end filling material in terms of lack of inflammation, presence of cementum and hard tissue formation.

Perforations

Furcation Perforation. Pitt Ford et al (39) were the first investigators who used MTA for repair of furcal perforations. They showed that cementum was generated underneath the material in most treated teeth, in contrast to the teeth whose furcation perforation sites were repaired with amalgam. These authors reported that when a perforation is left untreated for a period of time and becomes contaminated, the healing rate after perforation repair with MTA is significantly reduced. Yildirim et al (40) compared the healing of furcation perforations repaired with MTA versus Super EBA in dogs' teeth. Their findings revealed cementum formation underneath all MTA specimens at the 6-month interval, whereas Super EBA samples showed mild to severe inflammation around the repair material and no cementum formation during the same time interval. A study on dogs' teeth by Noetzel et al (41) showed significantly less inflammation in furcation perforation sites repaired with MTA after 12 weeks, as compared with those repaired with tricalcium phosphate cement.

Al-Daafas and Al-Nazhan (42) compared the biologic effects of GMTA with those of amalgam as furcation perforation repair materials on dogs' teeth with infected perforations. These investigators repaired the perforation sites with either MTA or amalgam and with or without the use of calcium sulfate as a barrier beneath MTA. The MTA specimens showed significantly less inflammation and greater bone formation compared with their amalgam counterparts. When calcium sulfate was used for preventing MTA overextension, mild to moderate chronic inflammatory cells, as well as stratified squamous epithelium, were observed around the perforation area. Vladimirov et al (43) repaired furcation perforations in dogs' teeth with ProRoot MTA or Titan cement and showed thinner capsules and fewer inflammatory cells in MTA specimens in comparison with the other material after 30 days.

On the basis of available information, it appears that MTA produces the best histologic results compared with other currently used perforation repair materials. In addition, placement of a barrier before MTA insertion has no significant effect on treatment success. Furthermore, repairing the perforation site before bacterial contamination is an important factor for successful treatment.

Lateral Perforation. A 2001 study on dogs' teeth by Holland et al (44) showed cementum deposition in many MTA specimens 30 days after treatment by using Sealapex and MTA for repairing lateral root perforations. After 180 days, most MTA samples exhibited cementum formation and no sign of inflammation, in contrast to Sealapex specimens that showed inflammation even after 180 days.

In 2007, Holland et al (45) intentionally induced lateral perforations in dogs' teeth after root canal therapy. They repaired these sites with MTA either immediately or 7 days later with and without pretreatment with CH. After 90 days, the immediately repaired group showed significantly better histologic results than the 2 other groups. On the basis of these results, they concluded that CH therapy before repairing a contaminated perforation does not improve the healing of a perforation site.

MTA as an Apical Barrier for Teeth with Necrotic Pulps and Open Apexes

In an investigation on dogs' teeth with immature apexes, Shabahang et al (46) induced periapical lesions and used osteogenic protein-1, MTA, or CH as apical barriers. The teeth in the MTA group showed a higher incidence of apical closure and fewer inflammatory cells than the other groups. In an experiment on monkeys' teeth with infected root canals and open apexes, Ham et al (47) used MTA or CH as root canal filling materials. Their findings showed that root canals filled with MTA had the highest amount of hard tissue formation and the lowest level of inflammation after 90 days. Because of the limited amounts of samples, the authors could not perform statistical analysis between the groups.

Felippe et al (48) determined the effect of CH on dogs' teeth with open apexes treated with MTA. Their results showed no significant differences in the formation of apical tissue barrier, bone and root resorption, and the presence of microorganisms between the groups. In addition, their findings determined that placing MTA without CH pretreatment results in more complete apical barrier formation compared with those pretreated with CH before placing MTA as an apical barrier. They further demonstrated that the amount of MTA extrusion was significantly higher in samples pretreated with CH compared with those without CH pretreatment.

These studies showed that MTA can be used as an apical barrier in teeth with necrotic pulps and open apexes with or without pretreatment with CH.

Orifice Plug Experiments

Mah et al (49) used WMTA as an orifice plug after complete root canal therapy in dogs' teeth. They reported no significant difference between the periapical responses in roots with and without MTA orifice plugs.

MTA as a Root Canal Sealer

A 1999 study by Holland et al (50) compared a glass ionomer root canal sealer (Ketac-Endo) with MTA as a root canal sealer in dogs' teeth. Their results showed that MTA consistently induces closure of the main canal foramen by new cementum deposition, with an absence of inflammatory cells after 6 months. In contrast, glass ionomer specimens displayed partial closure of the main canal foramen in some specimens and a mild inflammatory reaction around many roots.

In 2007, Holland et al (51) examined the influence of the extent of obturation on apical and periapical tissue response in dogs' teeth after filling root canals with MTA. Their results showed closure of the apex in 80% of their samples with hard tissue after 90 days and the presence of chronic inflammatory cells around the majority of periapical tissues.

On the basis of these results, it appears that MTA can be used as a root canal sealer, but overfilling with this sealer might have an adverse effect on periapical tissues. Further studies are needed to test MTA as a root canal sealer.

Animal studies of Other Types of MTA (Angelus MTA)

Gomes-Filho et al (52) compared the subcutaneous reaction of rats to Angelus MTA (AMTA) and light-cured MTA. AMTA specimens showed a minimal inflammatory response at 30 days and almost no inflammation at 60 days. Light-cured MTA specimens were associated with significantly more inflammation than AMTA and controls. Moreover, there was no sign of mineralized tissue adjacent to light-cured MTA samples.

Menezes et al (23) compared regular PC, WPC, GMTA, and AMTA as pulpotomy agents in dogs' teeth. Their results determined that all test materials were able to preserve pulp vitality and stimulate the formation of a calcified bridge.

Panzarini et al (53) used AMTA and CH for filling root canals in monkeys after immediate reimplantation. They observed no significant histologic differences between the 2 materials after 180 days.

The number of animal studies for various clinical applications of AMTA is very limited. More studies are needed to determine the efficacy of these substances.

Animal Studies of New Compositions for MTA

Holland et al (51) compared a mixture of MTA powder with propylene or distilled water as a root canal filling material in dogs' teeth. These investigators also compared the effects of intentionally overfilling root canals with MTA with fillings limited to the root canal space. Their findings revealed similar biologic responses to both mixtures. These authors reported significantly better results in specimens in which MTA was confined to the root canal space than in specimens with overfilled canals. Bortoluzzi et al (54) compared a mixture of WMTA powder with 10% calcium chloride (CC) or distilled water as pulpotomy agents in dogs' teeth. After 90 days, both groups showed favorable results in terms of hard tissue formation. However, the pulps in both groups showed the presence of mild chronic inflammatory cells and angioblastic proliferation.

The number of studies for various clinical applications of new compositions of MTA is very limited; more studies are needed to determine the efficacy of these materials.

Clinical Applications

A clinical comparison of repair materials is the ultimate and most reliable method for evaluation of their clinical usefulness and their long-term efficacy. MTA has been proposed as the material of choice for root-end filling (55), pulp capping (56), pulpotomy for primary teeth (57), apical barrier formation for teeth with necrotic pulps and open apexes (58), perforation repair (59, 60), and apexification (60). Numerous clinical investigations have been performed evaluating MTA for each one of the above-mentioned applications.

Vital Pulp Therapy

Several reviews have discussed the use of MTA as a pulp capping material (58, 61–64). These reports showed that MTA is a promising material for preserving pulp tissue when used as a capping material after partial or total pulpotomy.

Primary Teeth

Pulp Capping. The results from a case report and a case series study indicated that MTA can be successfully used for direct pulp capping of primary molars (65, 66). In a prospective clinical investigation of pulp-capped primary molar teeth either with CH or MTA, Tuna and Olmez (67) reported clinical and radiographic success after 24 months for both materials.

More clinical investigations are needed to support the use of MTA as a pulp capping material in primary teeth.

Pulpotomy. Many case reports, case series, and prospective clinical trial studies exist regarding the use of MTA for pulpotomy in primary teeth (66, 68–83). Eidelman et al (68) conducted the first investigation with MTA as a pulpotomy agent in primary molars. They reported no significant difference between MTA and FC.

In a randomized, single-blinded clinical study, Saltzman et al (70) showed no significant difference between primary teeth treated with FC-ZOE or diode laser and MTA pulpotomies. In a clinical investigation, Naik et al (71) showed no clinical and/or radiographic failures at 1, 3, and 6 months after pulpotomy with either FC or MTA. The authors noted tooth discoloration in 60% of the teeth treated with MTA as the pulpotomy agent. They dismissed this shortcoming of MTA by stating that the teeth were covered by stainless steel crowns after pulpotomy. Holan et al (73) compared GMTA and FC as pulpotomy agents in primary molars. The success rate in the GMTA group was 14% higher than the FC group. Because of a small sample size, the authors found no significant difference between the 2 groups after 4-month to 74-month follow-ups.

In a 12-month prospective clinical, radiographic, and histologic investigation that compared GMTA, FC, and WMTA, Agamy et al (69) found success rates of 100%, 90%, and 80%, respectively. Histologic findings in this study demonstrated that the quality of the calcified bridge beneath GMTA is superior to that beneath FC, and that the pulp architecture under GMTA is similar to normal pulp tissue.

Two separate case series investigations evaluated WMTA and GMTA as pulpotomy agents in primary molar teeth (75, 77). The authors reported that at 6 months, both types of MTA showed similar clinical and radiographic success. Percinoto et al (76) compared MTA and CH clinically and radiographically and found no significant differences between the 2 materials. It should be noted that the authors in this study did not follow the protocol that is recommended for clinical usage of MTA (84). Aeinehchi et al (79) as well as Farsi et al (72) compared MTA and FC as pulpotomy agents during 6 and 18 months in 2 separate clinical studies. They both reported more favorable results after pulpotomy with MTA in comparison with FC. In contrast to the findings of these studies, another study reported no significant differences in the clinical and radiographic success of teeth undergoing MTA or FC pulpotomy after a 24-month observation period (80).

Moretti et al (81) compared CH, GMTA, and FC as pulpotomy agents in primary molar teeth and showed significantly higher failure rates in teeth treated with CH. In contrast, a long-term clinical and radiographic study determined no significant differences between CH and MTA, ferric sulfate, and FC as pulpotomy agents (82). The results of a meta-analysis comparing success rates of pulpotomies using FC or MTA showed that MTA has significantly fewer failures compared with FC (83). Another meta-analysis of the results of current studies evaluating MTA, CH, and FC reported a more favorable success rate for MTA in terms of clinical and radiographic signs before tooth exfoliation (85). Pulp stenosis is reported as a common finding after pulpotomy with MTA (68, 69, 73–75, 77, 82). It should be noted that most investigations did not follow the clinical application of MTA placement for pulpotomy in primary molar teeth (68, 69, 73, 75, 76). Many of these studies used glass ionomer cement as a final restoration immediately after covering the pulp with MTA. In a pilot study, Nandini et al (86) used glass ionomer 15 minutes after MTA placement and showed a breakdown of MTA under glass ionomer. Most authors did not mention placement of a wet cotton pellet over MTA before placing the final restoration. More pulp calcification is reported in GMTA samples than in those treated with WMTA as pulpotomy agents (69, 75, 77).

Despite success with MTA as a pulpotomy agent in primary molar teeth, a recent survey in Ireland and the UK reported that 92.9% of pediatric staff of dental schools taught using ferric sulfate as a pulpotomy agent for vital primary molar teeth. This survey showed that staff taught the use of MTA only to the postgraduate students (87).

On the basis of current information, it appears that MTA can be used as a pulpotomy material in primary teeth.

Root Canal Filling. In a single case report, O'Sullivan and Hartwell (88) showed successful treatment of a primary molar that had no successor permanent tooth by using MTA as a root canal filling material.

Furcation Perforation. In a case report, Oliveira et al (89) illustrated the complete elimination of a furcation radiolucency and clinical success 20 months after treatment of a furcation perforation by using MTA in a primary molar tooth.

Resorption. In a case report, Sari and Sönmez (90) demonstrated complete resolution of a coronal third inflammatory resorption in a mandibular primary molar repaired with MTA.

In contrast to the use of MTA as a pulpotomy material in primary teeth, there is limited information regarding the use of this material as a pulp capping agent, root canal filling material, or in repairing perforations and repairing internal resorption in primary teeth.

Permanent Teeth

Vital Pulp Therapy. Several review articles have described the use of MTA for vital pulp therapy (58, 61–64, 91).

Pulp Capping

***Ex Vivo* Study—**In a recent study, Téclès et al (92) placed immature human third molar teeth immediately after extraction in a cell culture medium. They then exposed the pulps and capped them with either GMTA or CH. Immunohistochemical evaluation of the pulps capped with GMTA showed mineralization 1 day after exposure to this material. CH-treated samples initially exhibited no mineralization. However, after 14 and 28 days, similar foci of mineralization were observed in both groups.

***In Vivo* Studies—**Several review articles have been published regarding the use of MTA for management of traumatized teeth with pulp exposures (61, 63, 64).

Many case reports and clinical studies have shown successful outcomes after the use of MTA as a pulp capping agent in mechanically and cariously exposed pulps (56, 93–101). In a preliminary study, 14 intact third maxillary molar teeth that required extraction were capped with either MTA or CH after inducing standard pulp exposures (94). Histologic examination of these teeth at different time intervals showed dentinal bridge formation and mild chronic inflammation 2 months after pulp capping with MTA. Specimens treated with CH exhibited

the presence of irregular and thin dentin bridge formation after 3 months, with associated pulpal necrosis, hyperemia, and inflammation. The authors concluded that MTA is a better material than CH for treatment of mechanical pulp exposures.

A clinical prospective investigation on caries-free, human third molars compared WMTA with CH as pulp capping materials (97). No significant difference was found between the 2 groups in terms of clinical symptoms, superficial and deep inflammatory cells, pulp vitality, and the formation of a dentinal bridge.

In a case series study, Farsi et al (98) capped cariously exposed molar teeth with signs of reversible pulpitis by using MTA as a pulp capping material and followed them for 6, 12, 18, and 24 months. Ninety-three percent of the teeth showed clinical and radiographic success after 24 months. Another study compared histologic findings of intact, human third molar teeth capped with MTA or CH (101). All MTA-capped pulps showed dentin bridge formation. In contrast, only 60% of CH-capped pulps revealed hard tissue formation. MTA specimens showed significantly thicker dentinal bridge formation than those observed in CH specimens. With respect to the degree of inflammation, no significant difference was observed between the 2 groups. Nair et al (56) capped intact maxillary and mandibular third molar teeth with MTA or CH and followed them for 1, 4, and 12 weeks. Histologic findings in this study showed that most MTA specimens were free of inflammation after 1 week, whereas complete hard tissue formation was observed in many specimens at the 1-month time interval. In MTA-treated teeth, hard tissue formation at the capping area continued and advanced in length and thickness throughout the length of study. In contrast, CH-treated specimens showed less consistent hard tissue formation, presence of incompletely calcified bridges, and acute pulpal inflammation even at 3 months. In a long-term clinical and radiographic study, Bogen et al (99) reported a 97.96% success rate in teeth with carious exposures that were pulp-capped with WMTA or GMTA. These authors reported that the majority of the pulps (49 of 53) were capped with GMTA.

In a prospective histologic study, Sawicki et al (100) compared the effect of WMTA and CH as pulp capping materials on first and second premolar teeth that required extraction for orthodontic purposes. No significant difference was noted between the pulp capping agents in terms of their ability to form a dentinal bridge. However, there were significantly less superficial and deep inflammatory cells in the teeth treated with WMTA than in those capped with CH. Another investigation compared MTA with CH cement (Life) as a pulp capping material and reported a significantly higher incidence of calcified bridge formation with MTA after 30 days (102).

On the basis of available information, it appears that MTA is the material of choice for pulp capping in permanent teeth compared with currently used materials.

Partial Pulpotomy. MTA has been used successfully as a pulp capping material after partial pulpotomy (103, 104). Barrieshi-Nusair and Qudeimat (105) performed pulpotomies by using GMTA in 28 teeth with carious exposures. After caries removal and pulp exposure, the authors removed 2–4 mm of superficial pulp tissue and then covered the remaining pulp with GMTA. The patients were followed for 24 months. Seventy-nine percent of these teeth had normal responses to vitality tests, whereas 6 teeth were unresponsive. The authors reported no radiographic evidence of pathosis in any of their patients in this study.

In another prospective clinical and radiographic study, Qudeimat et al (106) compared CH and GMTA as pulp capping materials after partial pulpotomy in cariously exposed teeth. The authors reported no significant differences in radiographic and clinical success rates between the 2 capping materials. There are not enough studies to show the efficacy of MTA as a partial pulpotomy material in human teeth.

Pulpotomy. In a case report, Koh et al (107) showed successful treatment of dens invagination in 2 mandibular second premolar teeth. In a case series, Witherspoon et al (108) clinically and radiographically evaluated 23 symptomatic teeth that had MTA as a pulpotomy material for a mean recall time of 19.7 months. They reported that 15 of 19 teeth that were available for recall healed, and only 1 tooth had persistent pain. The authors categorized the remaining 3 teeth as healing specimens. In a histologic study, Chacko and Kurikose (109) compared CH and MTA as pulpotomy materials in premolar teeth that were scheduled for extraction for orthodontic reasons. Their results showed that the pulp-capped teeth with MTA had significantly less inflammation and better dentin bridge formation compared with those capped with CH.

El-Meligy and Avery (110) compared CH and MTA as pulpotomy materials in immature human teeth that were indicated for apexogenesis procedures as a result of extensive decay or traumatic injuries. The patients were followed clinically and radiographically for 3, 6, and 12 months. Of 30 cases treated (15 with CH and 15 with MTA), only 2 teeth that were capped with CH failed with associated pain and swelling. On the basis of these findings, the authors recommend MTA as a suitable alternative to CH.

In a case series study, MTA was used as a pulpotomy agent on cariously exposed pulps with a history of lingering pain. Histologic observations showed complete dentin formation 2 months after treatment in all of the treated teeth (111).

On the basis of available information, it appears that MTA can be used as a pulpotomy material in permanent teeth. More investigations are needed to prove its long-term efficacy.

Root-end Filling

In a review article regarding modern concepts in endodontic surgery, Kim and Kratchman (112) stated that MTA is the most biocompatible root-end filling material and can be used with predictable outcomes in endodontic surgery.

Case Reports. In a 2-year case report, Favieri et al (113) demonstrated a successful outcome for a maxillary lateral incisor with buccal cortical bone perforation treated with MTA as a root-end filling in combination with calcium sulfate and lyophilized bone as osteoconductive and osteoinductive materials.

Another case report illustrated a combined endodontic and periodontal approach for successful treatment of deep localized gingival recession with apex root exposure by using a subepithelial gingival graft and MTA (114).

Clinical Studies. In 2 separate prospective clinical investigations, Chong et al (115) and Lindeboom et al (116) compared IRM with MTA as root-end filling materials in single-rooted teeth and the mesiobuccal roots of maxillary molars. The results of both studies showed more favorable results with MTA, although they found no significant statistical difference between the 2 materials.

In a prospective case series study on 276 teeth with WMTA as a root-end filling material, Saunders (117) reported 88.8% clinical and radiographic success after 4–72 months. He concluded that using careful microsurgical techniques combined with MTA as a root-end filling material results in high success rates for endodontic surgery.

A recent clinical trial compared smoothing orthograde gutta-percha with placing WMTA as root-end filling material. Results showed significantly higher healing in the WMTA group after 1 year (118).

Presently, smoothing gutta-percha is not acceptable for treating teeth with periapical lesions during endodontic surgery (119).

Meta-analysis

A meta-analysis of 30 articles published in recent years indicated that MTA has a high clinical success rate, provides the best seal, shows superior biocompatibility, and is the only root-end filling material that promotes tissue regeneration when compared with amalgam, IRM, and Super EBA (120).

On the basis of available information, it appears that MTA can be used as a root-end filling material with a high success rate. More clinical investigations are needed to prove its long-term efficacy for this use.

Pain after Periapical Surgery

Two studies have investigated the incidence of pain and discomfort after the use of MTA as a root-end filling material (121, 122). The first study revealed no significant difference between IRM and MTA as root-end filling materials (121). The second study compared the amount of pain after periapical surgery by using WMTA as a root-end filling material or burnished gutta-percha (122). Their results indicated significantly more swelling in the latter group.

Perforation

Repair of root perforations with MTA is a clinical application of this material (84, 123, 124). Several case reports have shown successful treatment of furcation perforations with MTA (125–128). In a clinical and radiographic case series with MTA for the repair of various types of root perforations, Main et al (59) showed no pathologic changes after 12–45 months in all examined cases. In another case series, Ghoddusi et al (129) repaired mechanical or strip perforations with MTA and followed them clinically and radiographically for a period ranging from 6–12 months. Their results revealed that more than 82% of treated teeth displayed radiographic success, whereas all cases were symptom-free.

A recent case series investigated the prognosis of teeth with perforations in the furcation or within the cervical third of roots repaired with GMTA. They reported that 9 of 10 teeth healed after 5 years (130). Several authors have reported successful treatment of lateral root perforations repaired with MTA (129–136). Many used CH before MTA placement (129, 135, 136), whereas one author suggested using an absorbable collagen matrix to prevent MTA extrusion (133).

Another case report illustrated a mandibular second molar with both crown-root fracture and lateral perforation that was successfully treated by a combined treatment of MTA and polyacid-modified resin composites (Ionosite Baseline) (137).

On the basis of current information, it appears that MTA can be used for repair of root perforations with predictable results. Long-term clinical investigations are needed to prove its efficacy.

MTA as an Apical Barrier for Teeth with Necrotic Pulps and Open Apexes

Treating a tooth with an open apex and a necrotic pulp has always been a challenge for dental practitioners. CH has been used as the material of choice for apexification for many years (138). The main drawbacks of this procedure include its multiple scheduled visits and susceptibility of treated roots to fracture (138–140). There are many reports that disclose successful treatment of teeth with necrotic pulps and open apexes by using MTA as an apical barrier (141–155). Several review articles have also described clinical procedures with MTA as an apical barrier in teeth with necrotic pulps and open apices (148, 156–160).

Clinical Studies

In a comparative study on permanent maxillary incisors with CH or MTA, Pradhan et al (161) assessed the formation of a biologic apical barrier and demonstrated that the mean time for CH to form a hard tissue barrier is significantly longer than the time required for GMTA to induce a similar barrier. Another investigation compared WMTA with CH for treatment of teeth with immature roots and observed them for 12 months (162). None of the WMTA cases exhibited signs of clinical or radiographic failure, whereas 2 of 15 teeth in the CH group had tenderness to percussion and persistent periapical inflammation.

In a case series study, Pace et al (163) reported successful outcomes in 10 of 11 teeth with necrotic pulps and open apexes after application of MTA as an apical barrier after 24 months. In a prospective radiographic examination of 43 teeth with necrotic pulps and open apices, Simon et al (164) used either WMTA or GMTA as apical barriers and reported 81% success for these cases. The investigators in this study did not perform clinical evaluations of the cases, and they did not identify the success rates for each type of MTA. In another case series study, Sarris et al (165) used MTA as an apical plug in 17 incisors and followed them for a mean time of 12.53 ± 2.94 months. Of these, 94.1% were assessed as being successful clinically, whereas 76.5% were reported to be successful radiographically.

A recent case series evaluating 20 teeth with necrotic pulps and open apexes by using WMTA or GMTA as apical barriers for a period of 12–43 months (166) reported an 85% radiographic success based on periapical index scores (1 or 2) and an absence of clinical symptoms. The authors in this study did not identify the success rates for each type of MTA used in their study. Age, gender, initial versus retreatment, presence of periapical lesion before treatment, and differences in follow-up times had no significant influence on the outcome of teeth treated in this study. In a large retrospective clinical investigation on patients who had teeth with necrotic pulps and open apexes that were treated with MTA as an apical barrier, Witherspoon et al (167) showed no significant difference between the success rates of 1- or 2-visit treatments.

In a retrospective investigation, immature permanent teeth with pulp necrosis and apical pathosis treated with MTA achieved continued root development after proper short-term or long-term regenerative endodontic treatment procedures (168).

A recent survey by Mooney and North (169) showed that 86.3% of consultants in pediatric dentistry agree that the use of MTA as an apical barrier for immature permanent incisors with necrotic pulps is an acceptable method. However, half of these consultants would like to see more clinical evidence for the use of MTA as an apical barrier in these cases.

In 2 review articles Huang (170, 171) advocated the use of MTA for pulp regenerative procedures. Clinical reports showed encouraging results after treatment of teeth with necrotic pulp and open apexes by using this method for pulp regeneration (172–178).

Current data show that MTA can be used as an apical barrier in teeth with necrotic pulps and open apexes. More investigations are needed to prove its long term efficacy.

Resorption

External Resorption. Several case reports have described successful treatment of external root resorption by using MTA to repair these defects. The authors have used surgical, nonsurgical, or a combination of these approaches for treatment of teeth with external resorption defects (126, 179–184).

Internal Resorption. Successful surgical and nonsurgical treatment of internal resorption in both primary and permanent teeth has been reported in several case reports (90, 185–187).

Other Clinical Applications

MTA has been successfully used for the treatment of strip and supracrestal perforations, horizontal root fractures, sealing communications between the root canal space and external root surfaces, filling root canals of teeth with mature and open apexes, as well as management of dens invaginatus (59, 93, 107, 126, 145, 146, 188–206).

MTA has been used for treatment of internal and external resorptions, horizontal root fracture, and root canal filling material. More clinical data are needed to prove its long-term efficacy for these purposes.

In conclusion, despite using MTA in clinical applications for more than a decade, few clinical studies with a high level of evidence have been performed in comparison to *in vitro* investigations. Future investigations with a high level of evidence are needed to evaluate the actual effect of MTA in various clinical applications (207).

Clinical Studies of Other Types of MTA

Angelus white MTA (AWMTA) and Angelus gray MTA (AGMTA) have been successfully used to treat severe internal resorptive defects (208) and repair of root perforation, with some resultant discoloration (209). After replacing AGMTA with AWMTA, the authors reported no tooth discoloration 6 months after this procedure (209). Silveira et al (210) reported the successful healing of 2 accidental and carious furcation perforations after repair with AGMTA.

In a human dental pulp study, Accorinte et al (211) capped 40 permanent premolars with AMTA or CH powder and extracted them after 30 and 60 days. Their histologic findings established no significant differences between the 2 materials.

A pulp capping investigation compared GMTA with AGMTA in intact, caries-free human premolar teeth. Histologic evaluation showed no significant difference between either of the materials (212).

In a recent investigation, AGMTA and PC were used for pulpotomy in carious primary molars. None of the treated teeth showed radiographic signs, clinical signs, or symptoms of failure up to 24 months after treatment, although the teeth that were treated with PC showed significantly more pulp canal obliteration in comparison to the AGMTA group (213).

There are not enough studies to justify the use of AMTA for clinical applications yet.

Drawbacks

The main drawbacks of MTA include a discoloration potential, presence of toxic elements in the material composition, difficult handling characteristics, long setting time, high material cost, an absence of a known solvent for this material, and the difficulty of its removal after curing (71, 74, 76, 87, 157, 160, 169, 206, 210, 214–220).

Because of potential discoloration of teeth treated with GMTA, the manufacturer introduced a new formula of MTA with an off-white color (221). Three clinical investigations in primary teeth disclosed discoloration of teeth after using MTA as a pulpotomy material (71, 74, 76). One *in vitro* study has reported that all WMTA samples show discoloration 3 days after placing the material into a mold that was in contact with PBS (214). Boutsioukis et al (220), who evaluated the removal efficiency of MTA when used as a root canal filling material, discovered deep root discoloration in most specimens filled with AWMTA. Iron and manganese have been mentioned as possible elements responsible for this discoloration tendency (222, 223).

MTA contains many elements of PC including arsenic (224). In an investigation on arsenic release from MTA, Duarte et al (217) determined that the amount of arsenic released from MTA is very low. Investigations have assessed the total amount of arsenic in GMTA, WPC, gray PC (GPC), AWMTA, AGMTA, MTA-Obtura (AWMTA with a proprietary viscous liquid), CPM (Egeo, Buenos Aires, Argentina) (216), and MTA Bio (225). These studies showed that all tested materials have some arsenic in their composition. Monteiro Bramante et al (216) have reported that the amount of arsenic in GPC is 6 times more than that present in GMTA.

It should also be noted that the total amounts of arsenic in all types of MTA and some types of PC are insignificant according to the investigators' reports (225). The presence of ferric oxides in MTA (222, 226) and their stabilizing effect on arsenic in this material (227), the insolubility of MTA (228–231), and the use of small amounts of MTA for clinical applications should limit the release of arsenic into the tissue fluids that can potentially cause toxicity. However, the solubility of some PCs and release of arsenic from these materials have been raised as a matter of concern (230).

MTA has been considered as an alternative material to gutta-percha for root canal obturation. The drawbacks of using MTA as a root canal filling material include difficulty in obturation of curved root canals, discoloration potential, and long setting time (206).

A number of reports have complaints regarding the cost of MTA (157, 169, 218, 232). In a survey in the United Kingdom, 63.6% of consultants in pediatric dentistry were concerned about the cost of MTA and the instruments needed for formation of an apical barrier in teeth with necrotic pulps and immature apexes (169).

Some investigators believe that handling of MTA is not simple for some of its clinical applications and requires practice (169, 233), whereas other clinicians believe MTA is an easy material to use (234). A recent survey indicated that some students in the United Kingdom do not receive an opportunity to work with MTA before graduation (235).

The long setting time of MTA is one of the reasons that MTA should not be applied in 1 visit. This has been cited as one of the shortcomings of this material. Investigators have reported that WMTA has a significantly lower setting time compared with GMTA (215, 236).

There is no known solvent for set MTA (220). BioPure MTAD has been reported to partially dissolve WMTA when it remains in contact with the material for 5 minutes (237). However, thus far, no *in vitro* study has been performed to evaluate the effect of BioPure MTAD on MTA. Presumably, MTA cannot be removed from the root canal when it is used as an apical barrier or root canal filling material (160). An investigation using both rotary file and ultrasonic devices for retreating root canals filled with WMTA as a root canal filling material demonstrated the inability of these devices to completely remove set MTA (220). When the investigators used WMTA in conjunction with gutta-percha, using ultrasonic and rotary instruments left less WMTA on the root canal walls.

Despite its many advantages, MTA has some drawbacks such as a long setting time and discoloration of teeth. Efforts have been made to overcome these shortcomings; however, adding or removing various elements to alleviate these shortcomings can affect MTA's ideal characteristics. Introducing new compositions of MTA should await comprehensive investigations. New formulations have to be tested in *in vitro* as well as *in vivo* conditions before their applications in humans.

Mechanism of Action

One of the characteristics of a bioactive material is its ability to form an apatite-like layer on its surface when it comes in contact with physiologic fluids *in vivo* (238) or with simulated body fluids

in vitro (239). Apatite formation is a common characteristic of calcium silicate–containing biomaterials (240, 241). MTA is a bioactive material that is mainly composed of calcium and silicate (222, 226, 242–244). Investigations have shown that it can conduct and induct hard tissue formation (34, 245–256). Numerous investigators have illustrated the release of various ions from MTA when it is stored in liquid media (257–260).

Sarkar et al (258) filled root canals with MTA and placed them in contact with PBS for 2 months. They reported that MTA leached some ions in the following descending order: calcium, silica, bismuth, iron, aluminum, and magnesium. After resection of the root ends and examination of the samples under an optical microscope and then with SEM, the authors discovered the presence of a white layer between MTA and the root canal walls. Further examination of this white structure with energy dispersive analysis of x-ray revealed a structure composed of calcium, phosphorus, and oxygen and similar in composition to hydroxyapatite (HA). These authors stated that HA can release calcium and phosphorus continuously, a process required for bone metabolism. In addition, this phenomenon increases the sealing ability of MTA and promotes the regeneration and remineralization of hard tissues. On the basis of these results, Sarkar et al suggested that the biocompatibility, sealing ability, and dentinogenic activity of MTA result from the physiochemical reactions between MTA and tissue fluids during the formation of HA. Many animal studies that have analyzed the hard structure formed between the pulp-MTA interface have shown the presence of phosphorus and calcium, the main components of HA (9, 10, 20).

Bozeman and associates (259) confirmed the findings of Sarkar et al (258) by using GMTA and WMTA. They revealed that the amount of HA crystal formation over GMTA is more than that formed over WMTA. In addition, they reported the presence of lower levels of silica and phosphorus in GMTA crystals and more calcium ions in WMTA crystals. Moreover, GMTA releases significantly less silica in comparison to WMTA. The porosity in set MTA has been identified as a potential drawback for the material. It can allow the potential penetration of bacteria or their by-products; however, studies (258, 259, 261, 262) have shown that after MTA placement, a layer of HA forms over the material that fills the voids and surface defects. Formation of this layer develops a chemical bond between MTA and the dentinal walls that might be the key characteristic responsible for the successful performance of this material. A recent investigation reported that carbonated apatite forms over MTA, indicating the material's bioactivity. Carbonated apatite represents the mineral phase of hard tissues such as bone, cementum, and dentin and is known as a biologic apatite (263).

A recent investigation on the interaction between physiologic solutions and various types of MTA (AMTA, MTA Bio) reported that white precipitation forms over the material in the first hour after immersion in PBS, and it completely covers the surface of MTA after 5 days (263). In this investigation (263), formation of apatite crystals within the collagen fibrils has supported the reaction between MTA and dentin that finally forms a chemical bond (258).

The presence of various ions in an environment affects living tissues (260). The concentration of growth factors plays a significant role in hard tissue formation (264, 265). For example, a high concentration of transforming growth factor-β1 results in apoptosis and down-regulation of dentin phosphosialoprotein rather than a positive effect on tissue healing. One might assume that the production of transforming growth factor-β1 is a positive effect of a bioactive material in a cell culture environment. However, production of signaling molecules and ions should be at certain concentrations to be encouraging for cell viability and proliferation (241, 266).

Although production of HA is a very desirable phenomenon and a sign of biocompatibility, HA can induce cell death and inhibit cell proliferation when the concentration of Ca-P particles is too high. Midy et al (266) have shown that in the presence of high levels of Ca-P ions, osteoblast activities are down-regulated. In a cell culture investigation, Zhao et al (241) confirmed that the amount of extracts from a calcium silicate bioactive material needs to be at a certain concentration to encourage cell proliferation.

Studies have shown that placement of MTA on pulp tissue causes proliferation, migration, and differentiation of odontoblast-like cells that produce a collagen matrix (9, 17). The formed matrix is then mineralized and produces osteodentin initially and is followed by a tertiary dentinal bridge formation a few months after pulp capping. The mechanism of action of MTA is very similar to the effect of CH on pulp tissue after pulp capping.

In a recent study, Tomson et al (260) demonstrated that WMTA and GMTA release different signaling molecules from dentin powder that might influence their effect on the quality and the rate of calcified bridge formation. Killing *Enterococcus faecalis* with greater speed has been reported when dentin powder was mixed with MTA powder (267). Cementoconductivity and cementoinductivity of MTA have been confirmed when reasonable concentrations of the material (less than 20 mg/mL) have been used (268). A recent article has hypothesized that using MTA as an adjuvant material to fill the cavity of central giant cell granulomas after surgical curettage can induce both osteoconductive and osteoinductive effects and improve bone formation at the tumor site, as well as prevent recurrence of the tumor (269).

On the basis of current information, it appears MTA is a bioactive material and has the ability to create an ideal environment for healing. From the time that MTA is placed in direct contact with human tissues, it appears that the material does the following:

(1) Forms CH that releases calcium ions for cell attachment and proliferation (257–259, 266, 270–273);
(2) Creates an antibacterial environment by its alkaline pH (274–276);
(3) Modulates cytokine production (249, 250, 277–279);
(4) Encourages differentiation and migration of hard tissue–producing cells (17, 92); and
(5) Forms HA (or carbonated apatite) on the MTA surface and provides a biologic seal (258, 259, 263).

More investigations are required to determine the specific mechanism of action responsible for the bioactivity of MTA.

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