Clinical applications of hydraulic calcium silicate–based biomaterials in paediatric endodontics

KEY WORDS
Biodentine, calcium-enriched mixture, calcium silicate–based, CEM cement, endodontics, hydraulic calcium silicate cement, mineral trioxide aggregate, primary teeth, pulpotomy, vital pulp therapy

ABSTRACT
Nowadays, in order to prevent the early loss of cariously or traumatically damaged teeth in paediatric dentistry, different types of endodontic treatments are considered. Over the past decade, paediatric dentistry has primarily shifted its focus towards the preservation of vital tissues and improvement of treatment outcomes, and has benefitted immensely from the introduction of effective and safe bioactive endodontic materials. Since 1993, the year in which mineral trioxide aggregate was introduced, hydraulic calcium silicate–based biomaterials have made a significant impact on endodontic treatments. There is a growing body of evidence demonstrating that hydraulic calcium silicate cements are beneficial for both the least aggressive and most invasive type of vital pulp therapies, as well as for the management of non vital primary/permanent young teeth. Moreover, clinicians’ skills and knowledge regarding the applications of hydraulic calcium silicate–based biomaterials play a crucial role in achieving success with the applied methods. The objective of this review is to summarise the recent developments concerning hydraulic calcium silicate–based biomaterials and provide an overview of some existing trends alongside current theories that have significantly influenced the art and science of paediatric endodontics.

Introduction
Pulp capping, pulpotomy and pulpectomy are the standard procedures that are usually considered for endodontic treatment of primary teeth. The main goal of endodontic therapy is to properly manage the pulpal pathosis of primary or young permanent teeth by eliminating the microbial infection and associated inflammation, filling or obturating the cleaned canal space, and preventing any recontamination and reinfection of the root canal system of the tooth for its long-term function. In addition, based on the new concepts of minimally invasive endodontics (MIE), clinicians are expected to respect the original tissues, try to preserve vital tissues and focus on preventing disease from occurring and impeding its progress.

Modern endodontics has shifted to focus more on vital pulp therapies (VPTs) as a valuable minimally invasive approach. The primary goal of all VPT techniques is to preserve the remaining sound vital pulp tissue. The success of VPT depends significantly on the status of the remaining pulp tissue, good haemorrhage control, the use of a bioactive material and the presence of a bacteria-tight seal. When a bioactive material is to be employed, VPT techniques consist of specific treatments ranging from non-invasive stepwise caries excavation followed by indirect pulp capping (IPC), direct pulp capping (DPC), miniature pulpotomy, Cvek pulpotomy (also known as shallow, incomplete or partial pulpotomy) and full pulpotomy (also known as deep or complete pulpotomy) to partial pulpectomy, the most invasive form. Following a
pulpotomy, the vital pulp tissue cannot be preserved using traditionally employed toxic chemicals such as formocresol, which has been shown to cause fixation of the dental pulp11. After formocresol pulpotomy, no dentinal bridge is formed or observed and pulp inflammation occurs, which consequently leads to necrosis in the remaining dental pulp12. Since the start of this millennium, the risk of formaldehyde derivatives transferring to the other organs has raised considerable concerns because they are proven genotoxic and carcinogenic agents13.

Meanwhile, clot formation and fixation of the underlying pulp tissue are no longer the desired outcomes following pulp amputation in primary teeth, and the use of bioactive endodontic materials is strongly recommended as a biological alternative to these traditional approaches14.

Calcium hydroxide (CH) has long been the material of choice for pulp capping in both primary and permanent teeth. However, it has been shown to have two main drawbacks: unpredictable dentinal bridge formation, and hydrolysis15. To overcome these, Torabinejad16 introduced mineral trioxide aggregate (MTA) (ProRoot MTA; Dentsply Tulsa Dental Specialties, Tulsa, OK, USA) in endodontics. MTA, a hydraulic calcium silicate cement (HCSC), is an established biocompatible material. It has shown no irritating effects on the adjacent vital tissues, but has been proven to promote regeneration through dentinogenesis, cementogenesis and osteogenesis15,17-19. The main components of ProRoot MTA are tricalcium silicate, dicalcium silicate, tricalcium aluminate, bismuth oxide and calcium sulphate dehydrate20. However, MTA has also been found to have certain drawbacks, such as delayed setting time, discoloration potential and high cost (~$70/g)21,22.

In the past decade, several new HCSCs have been introduced for use in both primary and permanent dentition in order to overcome the disadvantages of MTA. These materials include calcium-enriched mixture (CEM) cement (BioniqueDent, Tehran, Iran), Biodentine (Septodont, Saint-Maur-des-Fossés, France), BioAggregate (Innovative BioCeramix, Vancouver, BC, Canada), BioRoot RCS (Septodont), Endo-CPM (EGEO SRL, Buenos Aires, Argentina), Endocem (Maruchi, Wonju, Republic of Korea), EndoSequence (Brasseler USA, Savannah, GA, USA), EndoBinder (Bindeware, São Carlos, Brazil), EndoSeal MTA (Maruchi, Wonju, Republic of Korea), iRoot (Innovative BioCeramix), MicroMega MTA (Micro Méga, Besançon, France), MTA Bio (Angelus, Londrina, Brazil), MTA Fillapex (Angelus), MTA Plus (Avalon Biomed, Bradenton, FL, USA), NeoMTA Plus (Avalon Biomed), OrthoMTA (BioMTA, Seoul, Republic of Korea), RetroMTA (BioMTA), Tech Biosealer (Isasan, Rovello Porro, Italy) and TheraCal LC (Bisco, Schaumburg, IL, USA)10. Some of these have been shown to be highly effective and reliable in the treatment of pulp in primary and young permanent teeth10,21.

It appears that CEM cement and Biodentine are supported by stronger evidence in the related literature and may therefore be recommended as the first choice after MTA23. They have also been used in a series of clinical applications other than VPTs, such as pulp therapy of primary teeth with severe resorption or regenerative endodontics for the management of non-vital immature permanent teeth, and yielded promising results24,25.

The major components of CEM cement are CaO (51.75%), SO3 (9.53%), P2O5 (8.49%) and SiO2 (6.32%) while the minor components are Al2O3, Na2O, MgO and Cl26. Since phosphorous is a major element in CEM cement, these indigenous phosphorous and calcium components enable hydroxyapatite to be produced independently from the external environment27. In contrast to MTA, CEM cement exhibits a surface composition comparable to dentine. Since hydroxyapatite is the main component of dentine, this similarity means that CEM cement also promotes cementogenesis and dentinogenesis28. In addition, the relatively short setting time of approximately 50 minutes is one of the advantages of CEM cement, along with its lack of discoloration potential and low cost (~$20/g)26,29.

Biodentine consists of two parts: powder and liquid. The powder part comprises tricalcium silicate, dicalcium silicate, calcium carbonate, oxide filler, iron oxide shade and zirconium oxide (radiopacifier), while the liquid part contains calcium...
chloride as accelerator, and a hydrosoluble polymer that serves as a water reducing agent. The setting time is around 12 minutes\textsuperscript{30,31}. The manufacturers claim that the material possesses mechanical properties similar to dentine and thus can replace it in case of coronal restorations. Biodentine demonstrates CH formation and calcium ion leaching, which are beneficial to the dental pulp\textsuperscript{32}. It has low staining potential and is available at a reasonable price (~US$10/capsule)\textsuperscript{33}.

The aim of this review is to provide a summary of the current best scientific evidence and an overview of some recent trends in HCSCs, specifically MTA, CEM cement and Biodentine, that have considerably influenced current concepts in paediatric endodontics.

### Clinical approaches for VPTs

Dental caries is still the most common infectious but non-communicable human disease. It is a biofilm induced disease that usually contains a polymicrobial flora, and is maintained by a dietary supply of fermentable carbohydrates\textsuperscript{34}; therefore, all techniques for treating caries lesions should focus on the destruction of microbial biofilm.

### Indirect pulp capping (IPC)

IPC is a procedure in which the deepest layer of affected or soft dentine is retained on the pulpal aspect of the caries lesion to avoid pulp exposure, while peripheral carious dentine is completely removed\textsuperscript{35}. The remaining lightly carious lesion should be isolated from the oral environment with an efficient pulp-capping agent and a proper restorative material. This nutrient deprivation inhibits further bacterial growth and subsequent invasion into the pulp, allowing acceptable recovery.

Maintaining pulp vitality and promoting biologically based management strategies are the primary goals in the management of deep caries lesions. Pulp exposure is best prevented by maximum care in radiographically diagnosed deep caries lesions. This can be achieved through selective caries lesion removal with a one- or two-visit restorative material. This nutrient deprivation inhibits further bacterial growth and subsequent invasion into the pulp, allowing acceptable recovery.

### Primary teeth

For decades, fast-setting CH was the most commonly used pulp-capping agent in the management of deep caries lesions. Due to its high alkalinity, CH has shown an antimicrobial effect on the remaining microorganisms in the affected dentine while inducing dentinal bridge formation\textsuperscript{37}. However, it has also exhibited hydrolysis behaviour, which could result in its ultimate disappearance\textsuperscript{38}. A unique meta-analysis and trial sequential analysis of randomised clinical trials\textsuperscript{39} did not find that lining with CH could be beneficial in the treatment of primary teeth. Therefore, CH lining for the management of primary teeth is not supported by sufficient clinical evidence.

On the other hand, a recent clinical trial\textsuperscript{40} revealed that the success of IPC is independent from the capping materials (CH or ProRoot MTA) and stated that the most important factors in successful IPC are avoiding bacterial recontamination and creating a bacteria-tight seal with a proper permanent restoration. New directions and treatment perspectives have indicated that IPC may now be recommended as an alternative to pulpotomy for treating primary carious teeth with reversible pulp inflammation\textsuperscript{41,42}. From a clinical perspective, however, studies need to focus on high-quality primary research investigating the efficacy of the management strategies in treating deep caries lesions\textsuperscript{43,44}.

### Permanent teeth

Adopting less invasive approaches is highly recommended to avoid any unexpected exposure of the dental pulp, including incomplete/selective caries lesion removal followed by IPC. A randomised controlled trial\textsuperscript{45} evaluated the effectiveness of IPC with either ProRoot MTA or CH. The trial investigated the thickness of the newly formed dentine in asymptomatic teeth in patients aged 16 to 34 years.
MTA was reported to have induced a thicker dentinal bridge in comparison to CH with a statistically significant difference at 3-month follow-up. Another randomised controlled trial revealed no statistically significant difference in the effectiveness of Biodentine when used as IPC material compared to glass ionomer cements in patients with reversible pulpitis. Long-term clinical and radiographic follow-ups have reported no superiority of Biodentine over glass-ionomer cements.

On the other hand, CEM cement was reported to have been successfully used to promote healing in the management of irreversible pulpitis associated with apical periodontitis in young teeth. A large case series and a randomised controlled trial also showed that CEM cement was highly successful in IPC management of deep caries lesions in mature permanent molars with clinical signs of irreversible pulpitis and the presence of apical periodontitis.

**Direct pulp capping (DPC)**

Exposure of human dental pulp is mainly due to deep caries lesion removal, dental trauma or iatrogenic mechanical exposure. DPC is a procedure in which the exposed vital pulp of pinpoint size is protected by placing a bioactive material directly over the site of exposure. DPC tends to seal off the exposure point while inducing positive changes at the tissue interface, namely the differentiation of stem cells to odontoblast-like cells and secretion of reparative dentine. The caries lesion is then restored with an appropriate restorative material to provide the necessary coronal seal.

Maintaining pulp vitality is considered a priority when managing deep caries lesions with pulp exposure in both primary and permanent teeth. This is achieved by minimising removed structure while allowing continuous repair or regeneration of the affected tissues.

**Primary teeth**

CH has traditionally been the pulp-capping material of choice for treating pulp exposure in cases where a small mechanical or traumatic exposure occurs in a primary tooth with normal pulp. However, DPC is one of the most controversial treatment options among VPT protocols for primary teeth, particularly in case of carious pulp exposure. The role of the capping agent used in DPC is also critical, as the main objectives are to eliminate further irritation or damage and to induce hard tissue formation. Most dental schools now encourage the use of MTA for DPC in primary teeth and no longer use CH for this purpose as it may cause internal root resorption and create tunnel defects.

A case report exhibited successful outcomes for DPC with MTA in a primary molar. A later case series reported the clinical response of primary teeth to DPC with MTA as promising; however, a variety of histological responses were noted, such as normal odontoblasts, irregular odontoblasts, intrapulpal calcifications, dentinal bridges, cementum formation, internal resorption, inflammatory infiltrate and pulp necrosis.

A split-mouth randomised controlled trial with two follow-ups showed high success rates in DPC treatment of carious primary molars using MTA or CEM cement, with potential for use in daily practice. The histological results of a randomised clinical trial exhibited hard tissue bridge formation associated with no inflammation in all CEM specimens after DPC. These findings indicate that if primary teeth are carefully handled following any type of clean exposure, exposed pulp will be highly likely to survive when covered properly and immediately with an appropriate endodontic biomaterial. Based on these pulpal responses of primary molars to DPC, it may be concluded that DPC with HCSCs could be considered a recurring trend in paediatric dentistry.

**Permanent teeth**

The consensus view on permanent teeth with mechanical exposure of asymptomatic pulp holds that they are successfully treated with DPC. A recent systematic review and meta-analysis confirmed that in intact permanent teeth undergoing experimental mechanical pulp exposure, CH was inferior to MTA. An immunohistochemical study on intact human teeth revealed that favourable
responses in dental pulp occurred after DPC with either ProRoot MTA or CEM cement, and dentinal bridge formation was stimulated.

VPT to treat carious pulp exposure in permanent teeth is a new trend, with research stating that such teeth can escape pulp extirpation when treated by DPC. Comparing the currently available capping materials, it appears that MTA is profoundly superior to the traditionally used CH due to its lower risk of failure. Further reviews and meta-analyses suggest higher success rates with MTA than CH in maintaining long-term pulp vitality, and thus less pulp inflammation and more opportunity for dentinal bridge formation. However, similar results were obtained when MTA was compared with other HCSCs, specifically Biodentine.

Interestingly, DPC with CEM cement was highly effective in promoting complete periapical healing in a mature molar tooth diagnosed with irreversible pulpitis associated with an apical lesion. This result indicated that the dental pulp should be viewed as a potent connective tissue with many more regenerative capabilities than has ever been traditionally considered.

The interrelations between inflammation and regeneration play an important role in the prognosis of VPT. It has been indicated that resin-containing materials might shift the dental pulp response more towards an inflammatory reaction due to their cytotoxicity, while resin-free materials, i.e. HCSCs, could induce pulp regeneration with an anti-inflammatory potential process.

**Miniature and Cvek pulpotomy**

Miniature pulpotomy is a surgical procedure with limited removal of dentine chips and damaged pulp, especially the injured odontoblasts after direct exposure of the dental pulp tissue not exceeding 1 mm. This treatment modality ensures a clean field, close and improved proximity and interaction between the capping biomaterial and stem cells. Cvek pulpotomy (also known as shallow, partial or incomplete pulpotomy) is a similar surgical procedure in which the damaged and inflamed coronal pulp tissue beneath an exposure site is removed to a depth of 2 to 3 mm to prevent the extension of the inflammation from affecting the rest of the coronal pulp, and can be considered in case of traumatic exposure. The application of an endodontic capping biomaterial over the remaining pulp tissue is essential in order to protect the underlying dental pulp before any restoration can be placed.

**Primary teeth**

Historically, in primary molars with coronal chronic pulpitis, partial pulpotomy with CH has shown favourable treatment outcomes compared to full pulpotomy. Considering the favourable success rate of partial pulpotomy, an MIE approach, and the potential cytotoxic effects of formocresol, researchers have recommended partial pulpotomy with CH instead of full formocresol pulpotomy in primary teeth with deep caries lesions. A clinical trial showed that the 1-year success rate of partial pulpotomy with MTA was approximately 91%, which is quite promising.

**Permanent teeth**

The status of the exposed dental pulp is an important factor that could influence and indeed alter treatment outcomes. There is a consensus that teeth with traumatic injuries or iatrogenic pulp exposure in asymptomatic patients have higher success rates than symptomatic teeth or cariously exposed pulp. However, a relatively new VPT procedure, miniature pulpotomy with HCSCs has demonstrated favourable treatment outcomes in the management of cariously exposed pulp with irreversible pulps associated with apical periodontitis and complicated crown fractures. In a case report, a symptomatic mature molar with carious pulp exposure was successfully treated a week after miniature pulpotomy with CEM cement. A recent randomised clinical trial compared the clinical and radiographic success of four VPT techniques for management of deep caries lesions in mature permanent molars, including teeth with clinical signs of irreversible pulpitis and presence of apical periodontitis. The trial revealed that the 12-month success rate of miniature pulpotomy...
with CEM cement was around 91%, and pulpal and periapical status had no effect on the treatment outcome.

Although partial pulpotomy is more aggressive than miniature pulpotomy, it is considered a more conservative method than full pulpotomy. In a clinical trial$^{81}$, partial pulpotomy with CH was performed on permanent molars with deep caries lesions and pulp involvement in patients aged from 13 to 27 years. The treated teeth showed dentinal bridge formation and were asymptomatic over a period of 26 months. However, the use of CH is still a controversial issue as the treatment outcomes are not predictable or consistent$^{82}$. A prospective clinical study$^{83}$ evaluated the outcomes of partial pulpotomy with MTA for carious pulp exposure of young permanent molars in patients with a mean age of 10 years. The study revealed that, over a 2-year period, MTA was an effective biomaterial. A recent systematic review and meta-analysis$^{84}$ concluded that partial pulpotomy could result in high success rates in managing carious pulp exposure up to 2 years. In addition, a 6 month follow-up could be advisable when wishing to assess the success of the procedure.

**Full pulpotomy**

Full pulpotomy involves the complete surgical removal of the coronal dental pulp to treat pulpitis in primary molars. This is followed by the application of a particular (bio)material directly over the pulp tissue at the level of the root canal orifices prior to the placement of a permanent restoration with a good coronal seal$^{4,35}$. It is clear that full pulpotomy is the most used of the various techniques for pulp management. It has long been regarded as the most reliable and successful technique in the treatment of primary and permanent teeth with pulp involvement$^{81,85}$. This technique is advocated as the approach best suited to preserving the surroundings for the future eruption of the permanent successor$^{86,87}$. Various methods are used with a wide range of (bio-)materials, from conventional pulp amputation with a sharp excavator and use of a sharp bur on a low-speed handpiece to the use of electrical cauterisation and laser surgical removal$^{72,88,89}$. The use of a fixation technique employing formocresol in primary teeth has long been recognised as the treatment of choice, with high clinical success$^{86,90,91}$. However, based on recent evidence, there has been a significant shift in paediatric dentistry to replace formocresol and CH with alternate native biomaterials for full pulpotomy in primary teeth$^{92,93}$. Pulpotomy is currently employed in 37 European dental schools, with MTA being the most popular biomaterial$^{56}$. In the new era, it appears that HCSCs are gaining momentum, and indeed their widespread use in full pulpotomy of primary and permanent teeth has clearly revolutionised the primary concept$^{5,81,88-91}$.

**Primary teeth**

Despite the clinical success of devitalisation as part of the formocresol pulpotomy technique, which was once the most commonly used treatment for retaining primary molars with pulp involvement, the adverse effects of formocresol, namely its carcinogenic, mutagenic and cytotoxic potential, raised concerns and led to investigations into alternative techniques and biomaterials$^{13,94}$. A unique histological and CBCT case study$^{95}$ reported that after full pulpotomy of a primary molar with CEM cement, a complete and thick calcific bridge with tubular dentine formed over canal orifices. This phenomenon was referred to as dentinogenesis and supports the healing potential of the dental pulp of primary molars after employment of an effective HCSC.

In recent years, many techniques and materials have been introduced to overcome the potential risks of using formocresol, including ferric sulphate, glutaraldehyde preparations, bonding agents, bone morphogenetic proteins, collagen electrosurgery and laser therapy$^{96-100}$. However, use of HCSCs has been highly recommended for full pulpotomy. Two systematic reviews and meta-analyses$^{101,102}$ have provided sufficient evidence to recommend the use of MTA rather than formocresol as a cytotoxic agent for full pulpotomy of primary molars. The latter stated that if the cost of treatment with MTA is problematic, especially when the treated
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... or the management of deep dental caries lesions and traumatic or carious pulp exposure of permanent teeth. In the last decade, it has been claimed that vital permanent teeth with complete or incomplete root formation after traumatic, mechanical or carious pulp exposure are suitable candidates for full pulpotomy.

For the management of vital immature permanent teeth with inflamed pulp, even in symptomatic cases, clinicians should always try to avoid apexification if apexogenesis with HCSCs is possible. Since a loss of vitality in the mentioned cases could leave short, thin and weak roots, apexogenesis is considered as the treatment of choice. A clinical trial reported that MTA, as a pulpotomy agent in the apexogenesis of immature permanent teeth, has shown better clinical and radiographic success in comparison with CH. A leading randomised clinical trial revealed that 100% of cases involving the use of CEM cement or MTA in pulpotomy procedures maintained pulp vitality and showed continuous root development. The study concluded that the use of biomaterials led to excellent treatment outcomes of full pulpotomy in immature permanent molars with carious pulp exposure. A recent systematic review and meta-analysis revealed that in the treatment of immature permanent teeth, similar success rates were found with MTA, CH and CEM cement.

In the past, the most commonly used treatment option for mature permanent teeth diagnosed with irreversible pulps was root canal therapy. However, understanding of the defensive responses of the dental pulp has deepened and a trend has emerged towards MIE, creating significant interest in VPTs, specifically full pulpotomy, in the management of such conditions. In 2009, a clinical trial showed for the first time that the treatment outcomes of full pulpotomy with CEM cement in 12 mature permanent molars with established irreversible pulps were successful at 15-month follow-up; the teeth were functional, with no signs or symptoms of pulp inflammation or infection. In another case series, ProRoot MTA was applied as the pulpotomy agent for the treatment of symptomatic cases. Histological observations showed that all samples displayed dentinal bridge formation and the pulp was vital and free of inflammation.

The largest prospective multicentre randomised clinical trial in the field of endodontics, conducted on over 600 volunteers, demonstrated that full pulpotomy with CEM cement could be considered a valid treatment option for mature permanent molars with irreversible pulps when compared to root canal therapy. In addition, evidence has shown that pulpotomy with CEM cement is highly recommended for general clinical practice. However, when full pulpotomies employing ProRoot MTA or CEM cement for such symptomatic teeth are compared, both biomaterials seem to show similar effectiveness. The performance of this novel approach in MIE may support a paradigm shift towards more biological and conservative treatments in dentistry.

To answer the question “which procedures and materials could be applied for full pulpotomy in permanent mature teeth?”, a systematic review concluded that while there is no evidence to support one single full pulpotomy procedure for different pulpal diagnoses, MTA, Biodentine and CEM cement are the first choices for such ministrations. A recent systematic review and meta-analysis regarding full pulpotomy for carious pulp
exposure in permanent teeth clearly stated that the success of pulpotomy in managing irreversible pulpitis challenges the widely held view that irreversible pulpitis can only be managed by root canal therapy. This could revolutionise the traditional beliefs in endodontics and perhaps encourage endodontists to change concepts, modify techniques and move rapidly towards the new era.

Management of nonvital cases

Immature permanent teeth

Nonvital immature permanent teeth present several problems for effective endodontic therapy. In such cases, the apex is usually significantly wide and there is no apical constriction to stop the root canal fillings from being pushed into the peri-radicular space and creating a 3D apical seal.

Apexification

Apexification is the traditional technique used to manage nonvital immature permanent teeth. In this technique, after the chemomechanical removal of necrotic tissues and bacteria from the root canal system, densely packed CH is used to induce a calcific apical barrier across the open apex. Apexification with CH offers predictable results, but has several disadvantages: it requires a 6- to 24-month period in order to induce the formation of an apical barrier, causes increased brittleness of dentine and amplifies the risk of cervical fractures. Nowadays, however, with the introduction of novel techniques and materials, the old CH apexification method is regarded as outdated.

One-step apical plug (artificial apical barrier) technique

An alternative treatment option to CH apexification is the insertion of an apical plug (artificial apical barrier technique). This has been defined as the nonsurgical placement of an endodontic HCSC biomaterial into the most apical portion of the root canal or the entire root canal(s) in one session. MTA and CEM cement are bioactive biomaterials with the capacity to induce cementogenesis when placed in contact with periradicular tissues. The cementogenic properties of these bioactive HCSCs may be related to their ability to set in the presence of moisture/blood, create a physical as well as biological seal, release calcium ions, conduct electricity, produce CH and form hydroxyapatite crystals at the material–tissue interface.

Several clinical studies have reported favourable treatment outcomes for MTA and Biodeentine apical plugs. Two clinical trials compared the treatment outcomes of MTA and CH apexification and concluded that MTA resulted in good success rates and thus could be considered an effective option for apexification, with the advantages of reduced treatment time, good sealing ability, biocompatibility and provision of a barrier for immediate obturation. HCSCs have already been validated as alternative biomaterials in the MTA apical plug technique. Similar to CH apexification, the apical plug technique using MTA or other HCSCs displays limitations and interruptions affecting root development, leading to increased risk of root fracture.

A systematic review and meta-analysis compared the efficacy of CH and MTA for the management of immature permanent teeth. The review concluded that both materials provide similar success rates; however, the shorter treatment time with MTA owing to better patient compliance may translate into higher overall success rates with MTA.

Regenerative endodontic procedures (revascularisation and revitalisation)

The new age of regenerative endodontics began with a case report by Banchs and Trope. Regenerative endodontic procedures (REPs) are biologically based procedures that allow the physiological replacement of the damaged tooth structures including dentine (through dentinogenesis), cementum (through cementogenesis) and the pulp–dentine complex. Currently, this field is at the cutting edge of endodontics.
Revitalisation involves ingrowth of tissue that may not be the same as the original lost tissue\textsuperscript{133}. Revitalisation is sometimes referred to as revascularisation due to the presence of blood supply. Researchers who prefer the term revitalisation state that the new tissue within the pulp space comprises blood vessels and vital cells, which are essential for the formation of the tissue. Therefore, the pulp space is filled with a type of vital connective tissue\textsuperscript{134}.

Several clinical studies\textsuperscript{135,136} have shown that REPs with MTA or Biodentine allow complete root development of immature necrotic teeth. The original technique recommends use of antimicrobial irrigants with non-cutting root canal instrumentation, intracanal antibiotic therapy with CH or triple antibiotic paste (TAP; ciprofloxacin, metronidazole and minocycline) and induced apical bleeding to form an intracanal blood clot and an intraradicular barrier to seal the root canal with a suitable HCSC\textsuperscript{129}. Although MTA is the most commonly used biomaterial to create the seal, current evidence\textsuperscript{129} suggests that all HCSCs are effective. They share most of their characteristics with MTA, but claim to have fewer drawbacks.

Two case studies\textsuperscript{130,137} compared the outcomes of REPs and apical plug in the same patients. The treated teeth were clinically asymptomatic and demonstrated complete radiographic healing of the periradicular lesions, but only REPs allowed root development. The surface characteristics of the set CEM cement are similar to human dentine, which might promote stem cell differentiation and induce hard tissue formation\textsuperscript{130,138}.

**Management of hopeless primary teeth**

Root resorption is considered as one of the main concerns in infected primary and permanent teeth\textsuperscript{67,132}. In primary molars with extensive root resorption and root perforation of endodontic origin, surgical tooth extraction and space maintenance are the treatments of choice. New procedures to preserve such teeth could help maintain their developmental, aesthetic and functional capabilities.

A randomised clinical trial\textsuperscript{139} compared the success of the repair of bony defects after the application of TAP combined with simvastatin (3Mixtatin) with MTA. The 2-year results showed that healing occurred more successfully in the 3Mixtatin treatment group compared to the MTA group. It was concluded that this might lead to a paradigm shift in the pulp treatment of primary teeth in the future. Another clinical study\textsuperscript{24} reported the results of perforation repair and deep pulpotomy treatment using CEM cement for primary molars with root perforations associated with a periodontal lesion due to extensive inflammatory root resorption. The follow-up examinations, up to 17 months, showed that all treated teeth were functional and asymptomatic and revealed complete periradicular bone healing. It seemed that the biomaterial had the necessary chemical composition to stop the resorption at its site and promoted its mineral replacement while eliminating all the inflammatory elements in the mechanical component of the treatment process.

**Conclusions**

Based on the concept of minimally invasive endodontics, an important factor in the improvement of endodontic treatment outcomes in primary and young permanent teeth is the preservation of the vital dental pulp. A paradigm shift is occurring in terms of the dental materials employed, and HCSCs have replaced traditional agents like formocresol and CH. Among the many HCSCs, MTA, CEM cement and Biodentine have stronger evidence, have been shown to be highly effective and reliable in VPTs, and have promising results in pulp therapy for hopeless primary teeth with severe resorption or even root perforation, and in REPs for the management of nonvital immature permanent teeth.

**Declaration**

The authors declare there are no conflicts of interest.
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