Review Article

# A paradigm shift from calcium hydroxide to bioceramics in direct pulp capping: A narrative review

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## Abstract

For many years, calcium hydroxide (CH) was the preferred material for direct pulp capping (DPC), occupying an elevated position. The collapse of this paradigm is due to the emergence of bioceramics with less pulpal inflammation and superior mineralization abilities than CH. The goal of the current article was directed to: (1) review the history of DPC "the idea of an exposed pulp as a hopeless organ has given way to one of healing and optimism," (2) classify the bioceramics in dentistry, and (3) explain and compare the mechanism by which dentin barriers for CH and bioceramics are formed. A comprehensive literature search of the database was conducted using PubMed, Google Scholar, and Scopus utilizing the following terms: Biodentine, calcium hydroxide, calcium aluminate, calcium phosphate, calcium silicate, direct pulp capping, NeoMTA Plus, Quick-Set2, and TotalFill. Reference mining of the selected publications was utilized to discover other studies and strengthen the results. Only works written in English were taken into consideration, and there were no restrictions on the year of publication. Bioceramic materials might be used as an intriguing substitute for CH. Compared to CH, they induced more positive pulpal reactions.

**Keywords:** Bioceramics; calcium hydroxide; direct pulp capping

## INTRODUCTION

The pulp is a distinct organ that is surrounded by a protective coating of dentin, which is surrounded by a layer of enamel. Pulp and dentin are identical embryologically, histologically, and functionally; because of this, they are also known as the pulp–dentin complex.[1] The pulp is a recognized reparative/regenerative organ capable of forming dentin in response to any lesion.[2] In contrast to reactionary dentin, which is generated by already existing odontoblasts, reparative dentin is created by exposing the pulp and rupturing the existing odontoblastic layers. The odontoblast-like cells are predicted to migrate, multiply, and eventually undergo odontogenic differentiation to generate reparative dentin.[3]

Direct pulp capping (DPC) is the process of treating a mechanically or traumatically exposed vital pulp by immediately capping the pulpal wound with a bioregenerative substance.[4] To properly seal the pulp perforation and prevent bacterial leakage, an optimal bioregenerative substance should induce the production of reparative dentin. If this procedure is effective, it eliminates the need for more invasive, complex, and costly root canal therapy.[5]

## LITERATURE REVIEW

### Calcium hydroxide

Rebel in 1922[6] conducted the first animal trials with terrible outcomes, leading him to believe that the exposed pulp was an organ doomed to failure. However,

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Date of submission : 14.04.2023
Review completed : 10.06.2023
Date of acceptance : 13.07.2023
Published : 13.01.2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jcde

DOI: 10.4103/jcd.jcd_241_23



**How to cite this article:** Al–Saudi KW. A paradigm shift from calcium hydroxide to bioceramics in direct pulp capping: A narrative review. J Conserv Dent Endod 2024;27:2-10.

it was Hermann's experiments from 1930[7] that presented calcium hydroxide (CH) as a good DPC agent in dentistry. The author showed how the dentinal bridging of the exposed pulpal surface was caused by the CH compound Calxyl. Since then, the focus has changed from the exposed pulp as a "doomed organ" to one of hope, recovery, and healing. The dentinogenesis that occurs after the DPC with CH is thought to be mediated by a number of processes, and no single mechanism can be thought in isolation.[8]

### *Role of wound injury*

The influence of surgical trauma was a factor typically not taken into account in the early researches. It seemed logical to suppose that the mechanical exposure damage itself and the subsequent release of inflammatory mediators would produce enough stimulation to aid in the dentin-healing process.[9]

According to classic research[10] evaluating the impact of germs on the outcome of surgically exposed dental pulps, the germ-free rats, which were housed in incubators, showed healing and a reparative response, leading to dentinal bridging despite suffering a significant surgical damage worsened by impaction of food and debris. In contrast, traditional rats' pulps, which were housed in cages, had significant inflammation before necrosis. No attempts were made to use therapeutic substances to alter the course of healing during this whole trial period. However, trials in which a thin layer of Teflon (inert material) was applied to pulpal wounds demonstrated the falsity of the hypothesis that the wound damage *per se* creates an enough driving force for dentinal regeneration.[11]

### *Role of pH*

It was proposed that an alkaline pH contributes to the production of reparative dentin since CH is a water-soluble molecule, it degrades when it comes into touch with pulpal fluid in tissues and generates hydroxyl ions ($OH^-$), raising pH to a level of 12.5–12.8.[3] CH may serve as a regional buffer to neutralize the inflammatory process's acidic responses. The lactic acid that osteoclasts release can be neutralized by an alkaline pH, which might help stop further mineralized tissue degradation. Alkaline phosphatase (ALP), which is thought to be crucial in the creation of hard tissue, may be activated by the high pH.[12]

ALP is a hydrolytic enzyme that works by releasing inorganic phosphatase from phosphate esters. Phosphoric esters can be separated, releasing phosphate ions, which subsequently interact with calcium ions ($Ca^{2+}$) to precipitate calcium phosphate in the organic matrix. The hydroxyapatite molecule can be found in such precipitate.[8] The pH required to activate this enzyme ranges from 8.6 to 10.3 (physiological pH level). However, it has been demonstrated that the pH of CH may reach 12.5, a value that is substantially greater than what is required for odontoblast preservation.[13]

### *Role of induced tissue necrosis*

Inflammation has been viewed as a negative outcome.[8] In fact, inflammation is necessary for pulp regeneration and tissue repair. The toxicity of CH induces a liquefaction necrosis in the pulp's outermost layers by the high pH and then quickly balanced as deeper layers of pulp are affected (coagulative necrosis). The nearby vital pulp tissue is only mildly irritated by the coagulative necrotic tissue. In the absence of microorganisms, this little irritation will cause an inflammatory reaction, which and lead to hard-tissue healing.[14]

The severity of the inflammation, the time of the irritation and bacterial contamination, and the site of exposure are all important variables in determining how quickly the inflamed pulp will be recovered.[15] Pulpotomized deciduous dentition with CH caps has been documented to have intrinsic dentin resorption, which happens if the pulp is chronically inflamed at the moment of therapy. Moreover, the pulp inflammatory response can be influenced by caries lesion, which is marked by a critical rise in the release of the pro-inflammatory cytokines such as tumor necrosis factor-$\alpha$, interleukin (IL)-1$\beta$, interferon -$\gamma$, CXCL8, IL-6, IL-18, and IL-10.[16] Hence, in clinical practice, it may be challenging to diagnose if the pulp is still alive or not under deep carious lesion. As a result, the pulp has to be partially or completely removed.[17] Inflammatory factors may be then resolved spontaneously and the pulp became fibrotic. A reactionary dentin that resembles bone may be formed as a result of mineralization that begins at the pulp's periphery. In this situation, reparative dentin may be also deposited and block the pulp perforation. In addition, calcifications may occur inside the pulp, creating endodontic therapy more challenging than if it had been done during pulp exposure.[18]

In a previous retrospective study,[19] carious pulp exposures that were capped with CH and restored with amalgam exhibited necrosis rates of 44% at 5 years and 79.7% at 10 years, whereas in a recent randomized clinical trial,[20] the accumulated DPC failures of 13.64% were observed in carious young permanent molars capped with CH following 1 week, 3 months, 6 months, and 12 months.

### *Role of calcium ions*

CH dissociates into $Ca^{2+}$ and $OH^-$ upon contact with aqueous fluids.[8] Continuous material dissolution creates a high $Ca^{2+}$ concentration local microenvironment, which is highest near the application site and decreases as directed away from the substance, generating a gradient that has the power to activate cells such as stem cells and the cells in reparative dentinogenesis that generate odontoblast-

like cells. Since these cells have calcium receptors, they may similarly function as sensors and trigger chemotaxis from deeper tissues to the damaged location. In addition, $Ca^{2+}$ has been shown to be a strong regulator of a number of other cellular processes, including mineralization, differentiation, and proliferation.[21]

### *Release of bioactive dentin components*

CH can release bioactive molecules that were previously trapped in the dentin matrix during the deposition phase.[22] The pulp cells of teeth have been demonstrated to reproduce, differentiate, and mineralize more readily when exposed to transforming growth factor. Fibronectin has been found to be localized to the dental basement membrane, where it promotes odontoblast polarization and cytoskeletal alterations. Bone morphogenetic proteins (BMPs) are crucial for odontoblast differentiation and dentin induction.[8]

### *Drawbacks of calcium hydroxide*

The nonadhesive nature of the CH and the gradual breakdown (disappearing Dycal syndrome)[23] may result in bacterial infiltration into the exposure site. Bacterial contamination can also arise due to flaws in dentin bridges, known as "tunnel defects" in dentin bridges, which can let bacteria travel from the exposure site to the pulp. The failure of operations is attributed to the impaction of pulp-capping agent particles, necrosing action that compromises pulp vascularity and obstruction by blood clot.[8]

## Mineral trioxide aggregate

Two US patents were acquired in 1993 by Torabinejad and White for a Portland cement (PC), afterward called ProRoot mineral trioxide aggregate (MTA) (Dentsply Tulsa Dental, Johnson City, TN, USA).[24]

### *Constitutions*

MTA is a type I PC derivative made of calcium silicate cement with a 4:1 proportion of bismuth oxide added for radiological dental diagnostics. The primary ingredients of MTA are 80% PC and 20% bismuth oxide. The anhydrate MTA material consists of 15%–25% silicon dioxide ($SiO_2$) and 50%–75% calcium oxide (CaO). Tricalcium silicate ($C_3S$), dicalcium silicate ($C_2S$), tricalcium aluminate ($C_3A$), and tetracalcium aluminoferrite ($C_4AF$) are created when these basic components are combined.[25]

### *Setting reaction*

The first reaction occurred between $C_3A$ and water; it led to the production of ettringite when gypsum was present. The major reaction between the $C_3S$ and $C_2S$ and water produced a weakly crystalline calcium-silicate-hydrate gel and CH. After the gypsum has been consumed completely, the $C_3A$ interacts with water to generate calcium-aluminate-hydrates. Gypsum acts as a retarder by forming a stronger diffusion barrier. However, water diffusion and swelling ultimately rupture the barrier layer, allowing basic hydration processes to resume more quickly.[26]

### *Setting time*

When compared to other dental materials, MTA takes the longest time to set. According to Torabinejad *et al*.,[27] the MTA setting time is around 2 h and 45 min.

### *Solubility and pH*

The set MTA exhibits less than a 3% weight decrease following 24 h when submerged in water. The mixture's initial pH is 10.2, and the pH increases to approximately 12.5 after 3 h of setting.[28]

### *Biocompatibility and bioactivity*

*In vitro* investigations show that MTA is a biocompatible material.[29] Sarkar *et al*.[30] discovered white precipitates on the MTA surface in a phosphate-buffered saline (PBS) solution. Scanning electron microscope (SEM) study of such precipitates indicated a spherical shape with calcium and phosphorus formulation of chemicals, while X-ray diffraction (XRD) investigation confirmed the existence of hydroxyapatite, which may stimulate MTA's dentinogenic activity by promoting reparative dentin formation.

### *Microleakage and sealing ability*

By preventing bacterial entrance at the interface, MTA seals perform extremely superiorly.[29] One potential explanation for MTA's sealing ability is its expansion after setting as a result of crystal development and potential gel hydration product swelling. Another possibility is related to the formation of crystals at the MTA interface, which would increase marginal adaption.[31]

### *Reparative dentinogenesis*

MTA stimulates dentin bridge formation similarly to CH, the CaO component of MTA interacts with tissue fluids to generate CH, which results in the formation of hard tissue.[29] It offers less pulp inflammation and thicker uniform dentin bridge creation with a superior nature (thickness, completeness, and integrity) compared to CH-based materials.[32]

MTA has also been shown to enhance the expression of transcription factors, including Runx2, which is implicated in molecular interactions during dentinogenesis. This may explain why it is more effective than CH at attracting of human dental pulp stem cells (hDPSCs) enhancing their migration, adhesion, proliferation, and differentiation for the creation of reparative hard tissues.[33] Moreover, MTA promotes angiogenesis and acidogenesis, but CH does not generate vascular endothelial growth factor expression, allowing for tissue regeneration.[34] In addition, it was reported that MTA enhanced BMP-2 protein synthesis,

which may play a crucial part in the mineralization and differentiation of odontoblasts, but CH decreased it substantially.[35]

### *Antimicrobial action*

The antibacterial action of MTA might not be as powerful as those of CH cement, but it does help to lower the bacterial load in pulpal injuries. It is possible that MTA's excellent sealing capacity will make up for its lower antibacterial activity.[29]

### *Limitations of mineral trioxide aggregate*

Some questions have been brought up regarding the incorporation of trace elements as PC is the primary component of MTA.[29] The calcium aluminate phase of the PC contains aluminum. Due to the risk of the potential of Alzheimer's disease caused by exaggerated exposure to aluminum in direct contact with human tissues, aluminum is not recommended in dentistry and biomaterials. Additionally bismuth oxide has been linked to tooth darkening from yellow to dark brown following reaction with sodium hypochlorite.[25] The setting time of around 2 h and 45 min[27] is a notable drawback of MTA. Due to this, pulp capping with MTA must either be completed in two steps, using a liner that sets up quickly to shield the MTA at the time of application the final restoration or by first applying a temporary restoration to provide the MTA time for setting. The powder–liquid MTA has very complex handling qualities. MTA is also quite costly. As a result, the development of bioceramic alternatives has been made to address the drawbacks of the initial MTA.[6]

## Biodentine

Biodentine (BD) (Septodont, Saint-Maur-des-fossés Cedex, France), often known as "dentin in a capsule," a "dentin substitute," with dentin-like mechanical qualities that have a favorable effect on living cells and work in a biocompatible way, is another increasingly attractive alternative for CH and MTA. Even in the chewing load-bearing zone, BD is able to be utilized as an interim filling lasting up to 6 months because it is sufficiently stable.[36]

### *Active Biosilicate technology*

It is preferable to produce pure synthetic tricalcium silicate (BD) in a laboratory rather than purifying natural tricalcium silicate (MTA) in clinker because the mineral contents are not affected by parameters for sintering or differences in the chemical constitution of the raw materials or include heavy metals. The sol–gel process is used in a laboratory to create the highly purified powder. Calcium nitrate and tetraethyl orthosilicate were utilized as precursors for CaO and $SiO_2$, respectively. The catalyst was nitric acid, whereas the solvent was ethanol.[37]

### *Chemical composition*

The primary constituents of the powder component of the material are $C_3S$ and $C_2S$, the first and second core components, with calcium carbonate serving as a filler. Zirconium dioxide serves as a biocompatible radiopacifier, whereas iron oxide acts as a coloring agent. The calcium chloride ($CaCl_2$) liquid acts as an accelerator. Water reducing agent based on polycarboxylate that has been adjusted to provide high short-term resistance.[38]

### *Setting time*

Grech *et al*.[39] used an indentation technique to assess the BD setting time while it was submerged in Hank's balanced salt solution utilizing a Vicat device and a needle with a particular mass. The amount of time from the beginning of mixing until the indentor fails to make a mark on the surface of the set material is used to calculate the mixture's setting time. The 45-min setting time for BD was established. The setting time is listed as 9–12 min on the product sheet from BD,[40] which is less time than was noted in the research by Grech *et al*.[39] who examined the final setting time, but the product sheet indicates that the initial setting time is between 9 and 12 min.

### *Bioactivity*

In the presence of PBS, the quantity of $Ca^{2+}$, silicon ions, and carbonate integrated from the BD to the surrounding dentin was measured, which proved the bioactivity of BD. The existence of structures which resemble tags that extend from the substance to dentinal tubules was discovered, resulting in the establishment of the referred to as "mineral infiltration zone," in which the neighboring dentin's collagenous component is destroyed by the alkaline byproducts of the material's hydration. Because of this deterioration, a porous structure is created, which allows high concentrations of ions to penetrate, resulting in enhanced mineralization in this location.[41]

### *Solubility*

BD was much more soluble than MTA at all experimental times according to the previous research by Kaup *et al*.[42] Theoretically, a substance that releases $Ca^{2+}$ needs to solubilize and dissociate from fully set cement to some level in order to have a biologic effect, leading to disintegration. The increased ion dissolution of BD compared to MTA may account for its higher solubility.

### *Microleakage and sealing ability*

The alkaline effect during the setting reaction is what gives BD its micromechanical adhesion. Organic tissues disintegrate out of the dentin tubule due to the high pH. The alkaline environment at the point where the hard tooth substance and BD come into contact creates a pathway to enter the exposed dentin canaliculi. Innumerable tiny microscopic cones can then be used to key BD to the dentin, resulting in a secure anchoring and a bacterial-tight closure.[41]

### *Reparative dentinogenesis*

According to a recent histological study[43] that compared the reaction of the human pulp to Dycal and BD as direct pulp-capping materials, after 45 days, the BD pulp-capped teeth were free of inflammatory cells and resulted in the creation of a fully calcified tissue barrier compared to Dycal pulp-capped teeth. On the other hand, both BD and MTA include calcium silicate in their chemical compositions and produce a similar pattern of pulp reaction.[44] The dentin bridge thickness, which was higher when using BD, was the sole factor that distinguished the pulpal response to MTA and BD.[45] This may be accounted for by the presence of calcium $CaCl_2$ in the BD liquid given by the producer. Despite the two substances creating identical chemical products, it is possible that the reaction in BD is more effective because of its shorter setting time. Furthermore, BD allows for a more release of bioactive ions ($Ca^{2+}$ and $OH^-$) through the first setting than MTA, lowering ion release with time and generating improvements to the pulp repair environment.[46]

## NeoMTA Plus

A contemporary bioceramic calcium silicate material called as NeoMTA Plus (NMP) (Avalon Biomed Inc., Bradenton, Florida, USA) provides CH for the creation of dentin bridges; it is thought to be an acceptable substitute for MTA for pulp capping.[47] To avoid postprocedural tooth discoloration, NMP uses tantalum oxide as a radiopacifier rather than bismuth oxide. Cement powder and gel are both components of NMP. Its powder contains smaller particle sizes than ProRoot MTA, which could be a factor in why it sets up faster, releases more ions, absorbs more water, and has less porosity. To enhance the handling qualities and washout resistance, the gel is blended with the powder until a putty-like consistency is achieved.[48]

### *Basic composition*

NMP comprises a fine powder of tricalcium silicate (alite), dicalcium silicate (belite), and calcium sulfate (as anhydrite), which was confirmed by environmental scanning electron microscopy and micro-Raman examination. The water-based gel lacks salts but does contain film-forming polymers and setting acceleration agents.[49] To reduce coronal tooth discoloration, tantalum is added to the NMP material as a radiopacifier.[50] Bismuth oxide, which is included in the majority of MTA-based cement, can discolor the coronal teeth, particularly when it touches with sodium hypochlorite.[49] According to ISO 6876:2012, NMP had a radiopacity more than 3 mm.

### *Setting reaction*

NMP undergoes a hydration reaction that results in CH as the first stage of its setting process. When this CH comes into touch with tissue fluids, it continues to react with phosphate ions to generate calcium phosphate hydroxyapatite.[51] Because aluminum accelerates the setting reaction, the inclusion of aluminum in comparatively high concentrations in NMP may be responsible for its quick setting noticed throughout mixing, when it hardens into a mass during a few minutes.[52]

### *Biocompatibility*

Fourier transform infrared, SEM, and XRD confirmed the existence of calcium phosphate precipitates on the surface of NMP following incubation in PBS for 15 days, which suggested that the precipitates formed could be a mixture of hydroxyapatite and calcium carbonate (calcite).[52] In human osteoblast-like cells, NMP has been demonstrated to boost ALP activity, which is produced as osteoblasts develop in their early stages and permit the evaluation of bioactive qualities of dental materials as well as their capacity to promote healing through mineralized tissue development. It also produced more mineralized nodules in an alizarin red test than MTA and TSC/$Ta_2O_5$ experimental tricalcium silicate cement with tantalum oxide.[53]

### *Bioactivity*

$Ca^{2+}$ and $OH^-$ ion release values from NMP were found to be greater than those from traditional MTA. The sustained release of $Ca^{2+}$ ions throughout the course of 28 days has been shown to be an important element in promoting tissue regeneration, which will increase the material's bioactivity and biocompatibility.[49] The early set materials' high solubility in distilled water is coupled with significant $Ca^{2+}$ and $OH^-$ release, which creates gaps. When NMP is submerged in bodily fluids, the materials' $Ca^{2+}$ and $OH^-$ ions mix with the phosphate in the surrounding fluids, causing the precipitation of a surface layer of calcium phosphate capable of filling the open gaps. This ability to create apatite may enhance the sealing of material-dentin contact.[49]

## Quick-Set2

Quick-Set2 (Primus Consulting, Bradenton, Florida, USA) is made up of a calcium aluminosilicate powder, a radiopacifier, and other proprietary ingredients combined with a one-of-a-kind water-based gel. Quick-Set2 is said to have a comparable quick setting time, ultimate pH, tubule penetration, acid, and washout resistances as its predecessors Quick-Set.[48]

### *Basic composition*

A silicate phase and calcium mono- and di-aluminate phases are both present in Quick-Set2 hybrid cement. While the silicate component is provided to facilitate mineralogic reactions, the aluminate phases in this hybrid cement provide acid resistance and short setting time.[54] Free alumina ($Al_2O_3$) and bismuth oxide are not included in this material. The proportion of the hydraulic phase rises with no free alumina present. The justification

for eliminating free alumina is based on the findings of earlier researches using *in vivo* pulpotomy and root-end filling that suggested free alumina might be a source of irritation to vital tissues.[48,54] To distinguish from dentin, Quick-Set2 contains a radiopaque powder. The possibility of discoloration is eliminated in Quick-Set2 by substituting tantalum oxide ($Ta_2O_5$).[54]

### *Biocompatibility*

Recent research[55] reported on the biocompatibility of Quick-Set2. Following two cycles of aging in deionized water, there was no changes in cytotoxicity of Quick-Set2. When cement was put in close proximity to undifferentiated hDPSCs, it was less cytotoxic than a zinc oxide eugenol-based cement. In a recent work,[54] the Quick-Set2 cement considerably improved the osteogenic differentiation of hDPSCs, with high ability for mineralogenic stimulation.

### *Reparative dentinogenesis*

A recent histological investigation[48] in a canine model demonstrated equal healing with Quick-Set2 or NMP, with the dentin bridge's quality being the only discernible variation. NMP showed higher dentin bridge quality after 90 days, which was better structured, with less cell or matrix inclusion. Organized tubules formed by underlying odontoblasts provide an excellent dentin bridge. These structured dentinal tubules may offer a better barrier than the amorphous calcified "dentin-like" tissue seen in pulp tissue beneath fast-advancing caries lesions. The chemical variations between the materials may explain the variance in bridge formation quality. The presence of free alumina particles in Quick-Set2 may have exacerbated inflammation. NMP and Quick-Set2 have maximal pH values of around 12 and 10, respectively. When calcium aluminates are present at the material-tissue interface, they have fewer $Ca^{2+}$ and $OH^-$ ions than tricalcium silicates, which may result in worse bridge quality throughout the healing process.

## iRoot SP

iRoot SP, a premixed, ready-to-use calcium phosphate silicate-based substance, was created in 2007 by a Canadian research and product development business (Innovative BioCeramix, Inc., Vancouver, Canada). These premixed bioceramic materials have been offered by Brasseler USA under the name EndoSequence in North America since 2008. Recently, FKG Dentaire, a Swiss company, has begun marketing similar materials under the name TotalFill.[56] The chemical components of the three types of bioceramics (calcium silicates, zirconium oxide, tantalum oxide, calcium phosphate monobasic, and fillers) are comparable.[57] The combination produces a crystalline structure resembling hydroxyapatite from teeth and is intended to improve the setting characteristics.[58] The physical and biological qualities of this cement are advantageous.[59] It comes in the form of a premixed putty or a paste, which is placed in a syringe that begins to harden if exposed to moisture.[60]

### *Setting reaction*

TotalFill's two main components are hydraulic calcium silicate and calcium phosphate monobasic.[61] TotalFill's setting response is activated by dentinal tubules' moisture.[62] Calcium silicate creates calcium silicate hydrate gel and CH when TotalFill is hydrated; calcium phosphate monobasic interacts with CH to produce calcium phosphate hydroxyapatite.[63]

### *Adhesion to dentin*

TotalFill's smaller particle size allows hydration improvement and consequent release of $Ca^{2+}$ and $OH^-$ ions, resulting in increased mineralization and high calcium phosphate deposition, as well as the formation of tag-like structures that extend into dentinal tubules, resulting in micromechanical anchorage.[64]

### *Reparative dentinogenesis*

No significant variations among TotalFill and NMP over the examination intervals were found by statistical analysis in a recent comparative histology investigation[65] utilizing TotalFill and NMP as DPC agents in human tooth cultures. TotalFill and NMP both resulted in positive pulp healing and repair. The only statistically significant difference between TotalFill and NMP after 3 months was dentin bridge thickness; TotalFill may build a thicker dentin bridge than NMP.

Along with its beneficial handling characteristics, TotalFill gives outcomes equivalent to BD in another histopathological study[66] using TotalFill, BD, and TheraCal as DPC agents in human tooth cultures. Regarding their outcomes in the three capping intervals (1 week, 1 month, and 3 months), there was not a statistically significant variance among them. Except for TheraCal LC, 25% of the specimens exhibited significant inflammation; this finding may be related to TheraCal LC's composition, which includes resinous monomers of bisphenol A-glycidyl methacrylate, hydroxyethyl methacrylate, and urethane dimethacrylate. If the free monomers are not polymerized, they can seep through dentin and reach the underlying pulp, where they might cause toxicity.

## Glass ionomer/resin-modified glass ionomer

When used near the pulp but without direct contact with it, glass ionomer also provides a great microbiological seal and strong biocompatibility. As a DPC agent, resin-modified glass ionomer demonstrated chronic inflammation and an absence of dentin bridge development, while the CH control groups demonstrated much improved pulpal healing.[67] The summary of the benefits and drawbacks of several pulp capping agents is described in Table 1.

**Table 1: Summary of the benefits and drawbacks of several pulp-capping agents**

| Pulp-capping agents | Benefits | Drawbacks |
|---|---|---|
| CH: Hermann, 1930[7] | Gold standard of DPC agent<br>Excellent antimicrobial properties (bacteriostatic after being initially bactericidal)<br>Low acid pH neutralization<br>Minimal cytotoxicity<br>Mineralization stimulation<br>Low price and not difficult to use[8,68,69] | Nonadhesive nature<br>High solubility<br>Disintegration over time<br>Deterioration following acid etching<br>Tunnels found in reparative dentin<br>Excessive dentin growth entirely obliterates the pulp chamber<br>Leakage at margin upon amalgam condensation[8,68,69] |
| MTA: Torabinejad, 1993[24] | Antibacterial property<br>Good cytocompatibility<br>Cells adhere and growth regulation<br>Bioactive dentin matrix protein solubilization<br>Limited inflammatory pulpal response and higher dentinal bridge formation compared to CH<br>No mutagenicity and toxicity<br>Radiopacity[29,68,69] | Difficult to manipulate clinically<br>Setting time is too long<br>Grey MTA results in postprocedural tooth discoloration<br>Two-step process<br>More expensive than CH[29,68,69] |
| BD: Septodont, Saint-Maur-des-fossés Cedex, France | Excellent cytocompatibility<br>Good antimicrobial activity<br>Compared to MTA, limited inflammatory pulpal response and higher dentinal bridge formation<br>Stronger mechanically compared to CH<br>Less setting time and better handling capabilities compared to MTA[37,68,69] | Need long-term clinical studies for a definitive evaluation<br>Higher cost than CH[37,68,69] |
| NMP: Avalon Biomed Inc., Bradenton, Florida, USA | Fine powder provides faster setting time than MTA<br>Gel enhances the handling qualities and washout resistance<br>Greater $Ca^{2+}$and $OH^-$ions release and lesser porosity than traditional MTA<br>Higher dentinal bridge formation compared to traditional MTA<br>No postprocedural tooth discoloration[49,68,69] | Early set material's high solubility creates gaps[49,68,69] |
| Quick-Set2 (Primus Consulting, Bradenton, Florida, USA) | Quick setting time<br>Ultimate pH<br>Tubule penetration<br>Acid and washout resistance<br>No postprocedural tooth discoloration<br>High ability for mineralogenic stimulation[54,55,68,69] | Low bridge quality compared to NMP[48,54,55,68,69] |
| iRoot SP (Innovative BioCeramix, Inc., Vancouver, Canada) | Premixed putty<br>Good antibacterial property<br>Less cytotoxic compared to MTA[60,61,68,69] | Small particle size for better hydration, and $Ca2^+$and $OH^-$ions release<br>Crystalline structure production resembles tooth hydroxyapatite by moisture absorption in the dentinal tubules<br>Higher dentinal bridge formation compared to NMP[60,61,68,69] |
| Glass ionomer (1995) | Excellent sealing ability<br>Similar to dentin in terms of coefficient of thermal expansion, and modulus of elasticity<br>Inherent adhesive nature to enamel and dentin<br>Good pulp tissue cytocompatibility[67,68,69] | Chronic inflammation over time<br>Lack of development of dentin bridges<br>Poor pulp tissue cytocompatibility<br>Unfavorable physical characteristics, an elevated solubility, and a sluggish setting time<br>RMGIC is greater cytotoxic than traditional GIC[67,68,69] |

CH: Calcium hydroxide, MTA: Mineral trioxide aggregate, BD: Biodentine, NMP: NeoMTA Plus, GIC: Glass ionomer cement, RMGIC: Resin-modified GIC, DPC: Direct pulp capping

## CONCLUSIONS

The treatment of accidental/mechanical vital pulp openings has shifted from using CH to bioceramic materials. Bioceramic materials might be used as an intriguing substitute for CH. Compared to CH, they induced more positive pulpal reactions.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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