ABSTRACT
Vital pulp therapy (VPT) in mature permanent teeth with carious pulp exposure has been a matter of debate, with root canal therapy being the conventional standard of care. Previously reported negative outcomes for VPT in these teeth were based on data from studies that have used calcium hydroxide in direct pulp capping and partial and full pulpotomy. The introduction of hydraulic calcium silicate-based materials with sealing and bioactive potentials have opened a new era in VPT with more favorable results. Understanding the histopathology and histobacteriology of the cariously exposed pulp and the healing potential of the inflamed pulp could guide the decision-making process toward an ultraconservative management of these teeth. However, proper case selection, strict aseptic condition, capping material, and good coronal seal are crucial for long-term success. (J Endod 2020;46:S33–S41.)

KEY WORDS
Caries; mature teeth; pulp biology; pulpotomy; vital pulp therapy

Epidemiologic studies consistently show a high global prevalence of dental caries, particularly in adults1. A prerequisite for any intervention intended to preserve the pulp is the presence of either healthy pulp tissue or pulpal damage that can be reversed. Inflammation of the pulp accompanies the carious process well before carious pulp exposure; however, the severity of the inflammation increases as the caries progresses toward the pulp. Nonetheless, even in the presence of carious pulp exposure, inflammation is typically limited to within 2 mm of the exposure site unless the carious exposure is of long standing, and it is not uncommon to find healthy pulpal architecture in the opposing pulp horn or further away in the pulp chamber2,3.

Historically, the use of vital pulp therapy (VPT) for mature permanent teeth with carious pulp exposure has been discouraged, with the majority recommending pulpectomy and root canal therapy4. The consensus that the pulp should be regarded as irreversibly inflamed whenever a carious exposure occurs in mature permanent teeth has been based on clinical outcomes of direct pulp capping with calcium hydroxide (CH). The biological rationale for this conclusion is that underlying pulpal inflammation has spread throughout the pulp and that the blood supply through a mature apex is insufficient to promote healing even after the insult is removed.

Significant improvement has occurred in the understanding of pulp biology and the response of the pulp to the carious process; the release of dentin-bound growth factors and active molecules such as stem cell factor, insulin-like growth factor binding protein, nerve growth factor, gial cell line–derived neurotrophic factor, and transforming growth factor beta 1 has highlighted the fact that the pulp in mature teeth has greater regenerative potential than what was previously thought5,6. Placement of bioactive materials, specifically tricalcium silicate-based materials (mineral trioxide aggregate [MTA], Biodentine, Bioceramics) has been shown to induce the release of these growth factors and to stimulate differentiation of odontoblast-like cells that modulate the inflammatory process and induce repair. The clinical use of these bioactive materials that provide a good marginal sealing has the potential to transform the management of carious exposures in mature teeth. The role of fibroblasts, which are abundant in the pulp tissue of adults, in modulation of repair and dentinogenesis has been recently highlighted7. Recent data have demonstrated that the pulp fibroblasts have an amazing anti-inflammatory potential through complement system activation8. Indeed, fibroblasts can directly kill cariogenic bacteria inhibiting the pulp by forming a membrane attach complex on their surface that induces their lysis9. Fibroblasts also produce other complement proteins such as C5a, which recruits macrophages, and C3b, which binds to pathogen surface, and stimulate their phagocytosis by the recruited macrophages10.
In this article we aim to review the pulp status beneath carious exposures and clinical management of mature teeth with carious pulp exposures from case selection to materials, clinical procedures, and outcomes.

PULPAL STATUS BENEATH CARIOUS EXPOSURES AND THE CLASSIFICATION OF PULPITIS

In carious teeth, the permeability of dentin is reduced by the presence of tubular sclerosis beneath the caries front. As the intensity of the bacterial insult increases, the inflammatory response intensifies, and the odontoblasts underlying the carious lesion are likely to die. Dental pulp possesses the innate ability to heal if the insult is removed 1; odontoblast-like cells replace lost odontoblasts and form reparative dentin. The origin of these cells has been under debate; mesenchymal cells have been implicated in their derivation 12. Regardless of their origin, these odontoblast-like cells secrete a matrix that is highly similar to that of primary dentin in terms of molecular composition and structure 13. If the carious insult is not removed, pulpal inflammation will progress and ultimately affect the entire pulp, resulting in pulp necrosis and apical periodontitis. The point at which the pulpal inflammation becomes irreversible even with removal of the stimulus has been debated for more than 50 years 2 and is essentially impossible to determine by currently available diagnostic tests such as thermal and electrical stimulation.

The terms reversible and irreversible pulpitis have long been used as part of the endodontic diagnostic scheme to guide the clinical decision-making process 14. However, the validity of these terms has been questioned — the terms have contributed to the poor outcomes with CH. On the other hand, pulpotomy in association with a bioactive material such as tricalciumsilicate cement is much more likely to lead to resolution of pulpal inflammation and preservation of pulp vitality, which would lead to a retrospective diagnosis of reversible pulpitis. In fact, numerous clinical studies have now been published on VPT with the newer materials, including pulp capping 16,17, partial pulpotomy 18 and full pulpotomy 19-22 with high success rates. These studies, which will be considered in more detail later, demonstrate the need for revision of the currently used diagnostic scheme. In our judgment, classification of inflammation of the pulp should be confined to “pulpitis” without any further designation.

MANAGING THE CARIOUSLY EXPOSED PULP

Vital pulp therapy has long been an accepted procedure for primary teeth and young permanent teeth, typically pulpotomy involving the removal of part or all of the coronal pulp. The concept of VPT for mature teeth is also long established, with almost a century of history behind its beginning when gold foil was used to cap exposed pulps 23. Calcium hydroxide became the material of choice after its introduction in the 1930s, typically as direct pulp capping over the carious exposure without removal of underlying pulp tissue 24,25. The poor long-term prognosis, perhaps resulting in large part from inadequate microbial control during the procedure and poor subsequent marginal seal, led to recommendations against its use for mature permanent teeth 6,26. It is possible to consider the pulp exposed carious teeth associated with irreversible pulpitis and hence there was the routine need for pulpectomy was the natural consequence of this observation. After the emergence of MTA as a root-end filling material 27, its proposed use in VPT was advocated 28, although it took 10 years for the first clinical reports of its effectiveness to emerge 29,30.

Numerous clinical studies with excellent outcomes have led to the need for a reconsideration of definitions of pulpitis (as discussed above), as well as the development of clinical protocols for case selection and management.

Despite the fact that root canal therapy performed for teeth with vital pulps has a high success rate when performed to adequate technical standard and under aseptic conditions 31, cross-sectional studies have documented the inadequate technical quality for root canal treatment to range between 30% and 60% across the world 32,33. The technically less challenging procedures associated with VPT make its adoption an attractive alternative to root canal treatment. In the following section we will summarize briefly some of the key steps in clinical management of the vital pulp derived from clinical studies using newer materials.

Case Selection

Age

Although most studies of VPT have been restricted to younger age groups, age does not appear to be a significant factor in outcomes of VPT 34-36. Preoperative signs and symptoms might be expected to serve as a guideline in the choice of VPT vs pulpectomy, despite the acknowledged limitations of both pain history and pulp sensibility tests 37. However, even some of the earliest studies of MTA involved teeth diagnosed with painful irreversible pulpitis (by traditional criteria), yet they resulted in predictable healing. Numerous clinical studies have since shown that painful pulps is not a contraindication to VPT. Ultimately an untreated carious exposure will lead to the progressive spread of pulpal inflammation and necrosis, but signs and symptoms do not necessarily reflect this progression.

Pulp Sensibility Testing

Cold testing is the most valid test for identifying necrotic pulps 38 and therefore continues to be essential before any attempt of operative work on teeth with deep carious lesions or lesions exposing the pulps.

Radiographic Assessment

Periapical radiography is essential for assessment of caries depth as well as periodontal health. Presence of periapical lesion in an inflamed vital pulp is not a contraindication for VPT, and several studies reported successful outcomes of pulpotomy in teeth with periapical lesions 21,22.
need of full pulpotomy until reaching a healthy architecture. 

The intensity of bleeding after pulp exposure has been suggested as an indicator for the severity of pulp inflammation. Profuse bleeding implies severe inflammation and indicates the need for further pulp tissue removal, with the hope to reach uninflamed tissue and achieve hemostasis.

**Microbial Control**

Whenever a carious exposure is suspected from the preoperative radiograph, complete caries excavation should be attempted under rubber dam isolation, followed by disinfection of the crown before caries excavation; most recent studies have included these precautions routinely. When the pulp is exposed, flushing the cavity with a disinfectant such as 1% NaOCl or chlorhexidine is encouraged to minimize bacterial load and prevent embedment of dentin debris into the pulp tissue, which may interfere with subsequent healing. Hemostasis after the pulpotomy procedure is often obtained by using low concentrations of NaOCl (1%–3%) on a cotton pellet 16,17,21,41,42. The difference in outcomes using NaOCl vs sterile saline has not been thoroughly investigated; only one randomized clinical trial in primary teeth reported improved outcomes of direct pulp capping after NaOCl hemostasis compared with saline 34. After VPT, the restoration must provide an enduring seal against microleakage.

**Extent of Pulp Tissue Removal**

Histologically in teeth with reversible pulpitis, bacteria are confined to the deepest dentin, whereas teeth with irreversible pulpitis have a necrotic area of varying dimensions. The intensity of bleeding is correlated with the area of necrosis. However, it is not possible to clinically determine the extent of pulp degeneration based on the clinical symptoms. Taking this into consideration will affect the decision on how much tissue should be removed.

The prognosis of VPT is dependent on the stage of pulp inflammation and the ability to minimize the insult and remove the inflamed tissue. Direct pulp capping in teeth of young subjects, without removal of pulp tissue, has an excellent short-term prognosis 18,19; an inherent disadvantage of direct pulp capping is that inflamed pulp tissue remains beneath the capping material. Even partial removal of the injured challenge can have a marked effect on clinical outcome; direct pulp capping and partial pulpotomy (Fig. 1) in adult teeth with carious pulp exposure have a success rate of 80%–85% during 2–3 years of follow-up in scenarios of symptoms of reversible or irreversible pulpitis (as conventionally defined 16,18,42,45). When full pulpotomy is performed, the success rate goes up to 90%–98% 21,22,30,46. A full pulpotomy to the canal orifices is technically less challenging than partial pulpotomy and may provide better restorative options (Fig. 2).

**Hemostasis as an Indicator of Pulpal Inflammation**

The association between the bleeding time and the degree of pulp inflammation has never been thoroughly investigated. Clinical studies with high success rates reported bleeding time between 1 and 10 minutes, with no significant association between bleeding time and outcome of VPT. In 84% of teeth with clinical signs and symptoms suggestive of irreversible pulpitis, vital pulp tissue was present clinically, and hemostasis could be achieved within 6 minutes after partial or full pulpotomy 18,22. The degree of bleeding on pulp exposure is not sufficient as a clinical index of the prognosis of treatment of pulp capping because of its low specificity by virtue that 55% of the cases with conspicuous bleeding were successful 16. Nonetheless, persistent bleeding despite attempts at hemostasis is considered a contraindication to VPT, and pulp capping is recommended 22,40.

**Materials for Direct Contact with the Pulp**

The ideal material for VPT should be able to resist long-term bacterial leakage and stimulate the remaining pulp tissue to return to a healthy state and promote dentin formation 15. Calcium hydroxide was the historical gold standard material for pulp capping; however, studies have shown the results to be variable and unpredictable, with success rates declining over time 26. Its use can no longer be recommended. Hydraulic calcium silicate-based materials (or tricalcium silicate cements) have shown superiority in outcome compared with CH; examples include MTA (Fig. 1) and non-staining fast set (12 minutes) Biodentine (Septodont, Sant-Maur-des-Fossés, France) (Fig. 2).

Biological properties of tricalcium silicate materials have been reported in several studies. They induce mineralization, cellular differentiation, and the release of dentin matrix components that up-regulate angiogenesis and the differentiation of odontogenic cells 8,49,50. On the other hand, resin-based composites or calcium silicate-based materials containing resin have shown negative effects on the dental pulp 61,52.

**Outcome Measures for Successful VPT**

Teeth that received VPT should be followed up both clinically and radiographically. Clinically the tooth should be asymptomatic, with no tenderness to palpation or percussion and no swelling or sinus tract, and it should be responsive to sensibility testing if it has received pulp capping or partial pulpotomy. However, in teeth with full pulpotomy no response to sensibility testing is expected, and in the absence of clinical and radiographic signs of failure we can assume that the radicular pulp is normal, and the treatment is successful. Radiographically there should be no signs of internal root resorption, no new periapical pathosis, and healing of periapical pathosis if it was present preoperatively 11,36,40.

**CLINICAL STUDIES**

Pitt Ford et al 23 first proposed the use of MTA for VPT, and its adoption for pulpotomy of primary teeth occurred rapidly 23. It took 10 years for the first case series in carious permanent teeth to be reported, involving both pulp capping 23 and pulpotomy 23, in both young and adult patients. Since those reports, clinical studies using several different materials (but all on the basis of similar chemistry described above) have investigated outcomes over a broader age range and clinical parameters (Tables 1–3).

**OUTCOME IN RELATION TO PREOPERATIVE SIGNS AND SYMPTOMS**

On the basis of reports from several clinical studies it has been proposed that root canal therapy is not a necessity after carious pulp exposure in teeth with signs and symptoms indicative of irreversible pulpitis 23. The outcome of pulpotomy in adult teeth with symptoms of irreversible pulpitis was favorable using CH 14, calcium enriched mixture (CEM) 22, MTA 19,21,30,47, and Biodentine 22, with success rates similar to those reported for conventional root canal therapy. Asgary et al 25 conducted a randomized clinical trial of pulpotomy using CEM for teeth clinically diagnosed with irreversible pulpitis compared with root canal therapy over 5 years of follow-up. The operators were general dentists, and comparable success rates were reported for the 2 procedures.

A recent systematic review (8 included studies) on pulpotomy of mature carious teeth with symptoms indicative of irreversible pulpitis
reported very high success rates: 97% clinical and 95% radiographic success rates at 1-year follow-up and 94% clinical and 88% radiographic success rates at 3-year follow-up. The lower success rate at 3-year follow-up was associated with studies that used CEM, whereas studies that used MTA maintained a high success rate after 3 years. In general, the outcome reported in systematic reviews of pulpotomy in teeth with signs and symptoms indicative of irreversible pulpitis is comparable to the outcome reported in a systematic review for teeth with reversible pulpitis and closed apices.

OUTCOME IN RELATION TO EXTENT OF PULP TISSUE REMOVAL

Among adults, direct pulp capping with CH yielded a low success rate of 35% after 1 year. A randomized clinical trial has shown that MTA is more effective than CH in capping carious pulp exposures in adult patients (85% vs 52%) over 3 years of follow-up, which corresponds with the findings of a meta-analysis of direct pulp capping and pulpotomy using CH or MTA. Pulps underlying a carious exposure will have a definite zone of inflammation beneath the exposure. Therefore, removal of affected pulp tissue is advised rather than simply placing material directly over the exposure by partial or full pulpotomy.

A recent systematic review and meta-analysis considered partial pulpotomy as a conservative treatment option for teeth with carious pulp exposure, with high success rate over 2-year follow-up, as long as the symptoms are indicative of reversible pulps. Their results were comparable to the success rate reported for full pulpotomy in teeth with a preoperative diagnosis of reversible pulpitis. The recommendation was to select partial pulpotomy because it is more conservative than full pulpotomy, and sensibility testing can still be performed at follow-up visits. Ten of 11 studies included in this review included young patients; only 1 study was limited to adults.

One randomized clinical trial reported the outcome of partial pulpotomy in teeth with symptoms indicative of irreversible pulpitis; the success rate was 85% over 2-year follow-up using MTA, which appears to be lower than that reported for full pulpotomy in similar situations.

Using a proprietary tricalcium silicate-based material, Asgary et al. reported on the outcome of VPT procedures including indirect pulp capping, direct pulp capping, and partial and full pulpotomy in mature teeth with variable clinical symptoms. All 4 VPTs were associated with favorable/comparable clinical and radiographic outcomes, and the pulpal and periapical status had no effect on treatment outcomes. Considering the different pulp status of cases included in this study (normal, reversible, irreversible pulpitis) and hence their different histologic and microbiological baseline condition, the results of this study might be taken with caution.

LENGTH OF FOLLOW-UP

Two-year follow-up has been considered adequate for direct pulp capping using CH and MTA and for pulpotomy using MTA, because failures tended to occur within this time frame. This period is probably not true for CH, because Barthel et al. documented the progressive decline over longer intervals in the outcome of CH direct pulp capping. Longer-term studies of 5–10 years would be helpful to confirm the recommendation of 2 years as sufficient follow-up. Whereas early failures reflect inaccurate assessment of the inflammatory status of the pulp, late failures usually reflect reinfection of the pulp space via a leaky restoration.

IS VPT A VIABLE AND EVEN PREFERRED ALTERNATIVE TO PULPECTOMY FOR CARIOUS EXPOSURE IN MATURE TEETH?

There is a great benefit in considering VPT outcome and regenerative endodontics with respect to the goals of patients, clinicians, and scientists. In terms of patient-related outcome, the prompt reduction in pain levels after pulpotomy, for example, reaches 95%.
which is well-received by the patient\textsuperscript{41,61}, the tooth is functional, and daily activities and quality of life are undisturbed.

Recommending minimally invasive dentistry reduces overtreatment and the restorative cycle by preserving tooth structure, while being cost-effective. A cost-effectiveness analysis has shown direct pulp capping to be superior to root canal treatment if the cavity is class I and the patient is a young adult\textsuperscript{62}.

Considering the advantages of VPT in class I and the patient is a young adult\textsuperscript{62}, the tooth is functional, and daily activities and quality of life are undisturbed.

FUTURE RESEARCH NEEDS
A diagnostic scheme should contain only categories that can be differentiated by signs and symptoms plus diagnostic tests; otherwise, there would be no clinical value for such a scheme or multiple subcategorizations. Current pulp testing is not reliable to the extent that determining pulpal status has been described in any clinical study as yet. On the other hand, restorative options may be more restricted after VPT than with root canal therapy, because the pulp chamber and canal space are not available for retention.

The high success rate reported for VPT procedures using calcium silicate-based materials (MTA, Biodentine, CEM) in mature permanent teeth with carious pulp exposure over medium- to long-term follow-up provides an evidence-based background for the adoption of VPT in these cases. The use of appropriate material and technique may allow the pulp to heal in adults at least as evident radiographically and clinically.
of the markers that reflect matrix degradation are actually required for repair as well\(^{40,63}\). Efforts should be directed to introduce a new way for diagnosing pulpitis and relate this diagnosis to minimally invasive treatment choices of VPT that are based on the degree of pulp inflammation.

The limits of VPT also need to be addressed more fully in relation to patient age, previous caries and restorative history, depth of carious lesion, time to achieve hemostasis, pain scores and severity of symptoms before treatment, and type of definitive restoration after VPT in long-term clinical trials. Because of the history of direct pulp capping with CH and the progressive failure of this treatment over a prolonged period\(^{26}\), follow-up studies should be conducted over at least 5 years if possible.

The best studies on VPT are based on 1-arm prospective studies, which may carry a high risk of bias\(^{46}\); randomized clinical trials on VPT for cariously exposed pulps using CH are currently not feasible because of poor outcomes\(^{16,18,42}\). The only possible design is to compare different calcium silicate materials or comparative clinical trials for VPT and root canal therapy to further support the adoption of VPT, particularly in mature teeth with clinical symptoms suggestive of irreversible pulpitis.

Partial and full pulpotomy are associated with different levels of pulp preservation. In the literature there is no consistency with regard to the indications of each procedure; both procedures have been performed interchangeably without consideration of the pathologic status of the remaining tissue\(^{17}\). Further studies comparing these procedures in teeth with similar preoperative clinical diagnosis and possibly using direct clinical observation of the exposed pulp are needed.

Although the newer materials based on hydraulic silicate cements (tricalcium silicates) have resulted in excellent results to date, the possibility of incorporating bioactive agents into cements may further enhance healing. Examples of these bioactive agents may include previously extracted dentin matrix\(^{64}\) or pharmaceuticals that modulate stem cell differentiation and the rate of dentinogenesis by modulating the p38 mitogen-activated protein kinase and the histone deacetylase\(^{64}\). It will be difficult to demonstrate that such bioactive molecules would lead to improved outcomes over already available cements that are highly successful.

**CONCLUSIONS**

- Maintenance of pulp vitality by the adoption of minimally invasive procedures is highly encouraged in adult teeth with carious pulp exposure.
- Parallel with the need for an update of the diagnostic terminology of the state of the pulp, there is an urgent need for more representative pulpal diagnostic methods.

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