Contemporary Endodontics for Children and Adolescents

Anna B. Fuks
Moti Moskovitz
Nili Tickotsky
Editors

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Preface

As the corresponding editor of the Pediatric Endodontics book, which was an excellent seller and was even translated into two languages, one of them Chinese, I was asked by the Springer representative if I would consider editing a second edition. As many new techniques and materials have been developed in the last five years, and due to issues not related to this book a second edition was impossible, we decided to publish a new, up-to-date book with a broader spectrum. I felt this was a big enterprise to undertake by myself, so I invited two experienced colleagues, Prof. Moti Moskovitz and Dr. Nili Tickotsky, to join me as co-editors of the new book. The chapters were all written by highly qualified experts.

The book we present here describes pulp therapy for children and adolescents from a holistic approach that highlights the new developments in the field. It has two parts: the first updates the readers on the biological aspects of pulp therapy, and the second deals with a wide range of clinical aspects.

In the first part, we describe the formation, structure, and function of the dental pulp as revealed by the latest single-cell visualization technologies. We then thoroughly discuss carious lesions and their impact on the pulp.

The second part examines the clinical considerations in the decision to perform pulp treatment. We emphasize the need to integrate pupal diagnostics with patient-dependent factors such as behavior management and pulpal pain mechanisms. This part of the book includes comprehensive descriptions of current treatments for each type of caries-inflicted tooth damage, from selective caries removal through direct pulp capping, pulpotomy, pulpectomy and root canal therapy for the primary dentition to direct pulp capping, and endodontic treatment of young permanent teeth. We describe both traditional and new pulp treatment materials and the techniques and materials used to restore both primary and young permanent teeth and summarize innovative biological approaches for pulp regeneration such as the use of stem cells.

We hope that both dentists and students will benefit from the expertise and knowledge this book contains and from the holistic approach it advocates.

Jerusalem, Israel — Anna B. Fuks
Jerusalem, Israel — Moti Moskovitz
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1 Introduction: Pulp Therapy for Children and Adolescents – Historical Approach, Present Perspective, and Future Directions

Anna B. Fuks, Moti Moskovitz, and Nili Tickotsky

Contents

1.1 Introduction

Pediatric dentistry evolved from an extraction-oriented approach, where primary teeth with inflamed pulps were mainly extracted, with no attempt to preserve the tooth and the pulp, to a specialty emphasizing prevention of oral and dental diseases [1].

Historically, pediatric dentistry was based on three pillars:

1. Stopping the progression of early childhood caries (ECC) by implementing restorations, pulp therapy, and extractions.

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2. Establish prevention regimes to stop the recurrence of the disease.
3. Develop regular care protocols to ensure good oral health through adulthood [2].

The preventive tools in pediatric dentistry had remained the same for years and included a four-part manifest that advocated drinking fluoridated water, brushing teeth with fluoridated paste, eating a low-sugar diet, and visiting a dentist twice a year.

In the last few years, preventive measures have been based on the child's and family's caries risk assessment (CRA), leading to a more promising and useful chairside diagnosis that emphasizes individualized patient-centered care [2].

With the improvement in diagnostic criteria and the appearance in the market of new dental products and materials, better and more conservative approaches have been developed, including esthetic and sophisticated restorative techniques that are part of contemporary pediatric dentistry [3].

However, social changes are occurring at an extremely rapid pace, and it is imperative to accommodate them with new information. Children are changing, and so are their parents and dentists. A new generation of young pediatric dentists may not accept the traditional methods to manage and treat their patients while dealing with their accompanying parents.

The current tendency is to avoid using aversive techniques, which were traditionally employed by pediatric dentists in the past. Consequently, there is an increased use of deep sedation and general anesthesia for the dental treatment of children [4].

In 2017, the US Food and Drug Administration published a warning that general anesthesia in children less than 3 years of age should be avoided, as it may affect their neurological development. This observation led several European and South American pediatric dentists to start using less invasive restorative techniques for young uncooperative children. Presently, the use of conservative techniques such as ART (atraumatic restorative technique), silver diamine fluoride (SDF), and the Hall technique, as a temporary or definitive treatment is increasing worldwide [5].

The conservative approach goes further regarding pulp therapy. It has been established long ago that the human dental pulp has a remarkable potential for self-healing when encountering severe damage, particularly in young patients, mainly due to the high degree of cellularity and vascularity. In addition, pediatric endodontics, which treats the pulp of primary and young permanent teeth, has its considerations and characteristics and must always be considered in the context of both the dentition and the patient.

This book has two main purposes: the first is to emphasize the changes leading to the conservative approach to restorative and endodontic techniques, and the second is to discuss the various clinical treatment techniques for primary and young permanent teeth.

1.2 Historical Perspective: Personal Approach

The first mention of capping an exposed pulp with gold foil was described by Philip Pfaff, a dentist at the court of the Prussian king Frederick II, in Berlin in 1756. At that time, the current belief was that the pulp must be irritated by cauterization in order to heal and several materials were used empirically. At the beginning of the twentieth century, it became obvious that microorganisms were the main reason for pulp inflammation. More attention was paid to finding effective disinfecting agents, some of which were very cytotoxic [1].

The difficulties in achieving accurate diagnoses led to a deficient assessment of pulp status that in turn led to the selection of incorrect treatments. In fact, necrotic pulps were sometimes capped [3]. Hermann studied the reaction of vital tissue to calcium hydroxide in root canal fillings between 1928 and 1930 and proved it was a biocompatible material [1].

As one of the few remaining members of the first generation of pediatric dentists and the senior editor of this book (ABF), I felt it would be interesting to comment on the changes I have experienced during my teaching and clinical career in pedodontics, later named pediatric dentistry.

As a young practicing dentist who did not have enough theoretical and practical experience in behavior management of children, I was more afraid to administer a local anesthetic on a child than the child was afraid of "getting a shot." So, when I needed to treat a tooth with a deep cavity and expected low compliance, I would use a devitalization paste before performing a pulpotomy. The devitalizing agent, in addition to causing intense pain, when improperly placed into the cavity, could cause gingival inflammation and even bone necrosis. I was aware that the use of this approach is empirical and has no scientific background, so I searched for relevant literature and was surprised to find a university-based paper from 2017 discussing the advantages and disadvantages of available methods for the treatment of pulpitis, including mortal endodontic treatment!!! [6]

As a resident at the Children's Hospital at the University of Alabama, I had encountered different clinical problems and had to find a way to solve them; this is how my interest in histology and pulp therapy evolved.

In the early seventies, already teaching clinical pediatric dentistry at the Department of Pedodontics of the Hadassah School of Dental Medicine in Israel, where I still belong as professor emeritus, I would write in a treatment plan "possibility of a pulpotomy" if deep caries were disclosed in the middle third of the cavity in the preoperative radiograph. This approach was not accepted in some universities, and the argument was that even in shallow proximal cavities or middle-third occlusal cavities, the pulp was inflamed and had to be treated by pulpotomy. Some serious discussions developed among pediatric dentists on this subject, and many didn't accept the concept that pulp inflammation was reversible if the tooth was properly restored without marginal leakage.

Controversies existed also regarding materials for pulpotomy: calcium hydroxide was initially recommended as the material of choice for primary teeth pulpotomies. However, as many cases of internal root resorption were observed after calcium hydroxide pulpotomies, formocresol became the preferred pulpotomy dressing material worldwide, and calcium hydroxide continued to be used mainly in the Scandinavian countries.

Several materials have been proposed to replace formocresol for pulpotomies in primary teeth, and nowadays, bioactive bioceramic materials are preferred, in cases where more conservative treatment was not possible.

Two treatments that have been established in the last years are indirect and direct pulp treatments, both of which were historically unacceptable for primary teeth. Indirect pulp was recommended only for deep cavities in young permanent teeth, preferably in a two-stage technique.

I am pleased to have survived and continued in pediatric dentistry to see the development of a biological and conservative approach to treatment and for being able to publish this book with the help of the most prominent members of dentistry and biology.

1.3 Present Perspectives

This book aims to familiarize dental students as well as general practitioners and pediatric dentists with the different modalities of pulp therapy for children and adolescents from a holistic approach that highlights the new developments in the field. It has two parts: the first updates the readers on the biological aspects of pulp therapy, and the second deals with a wide range of clinical aspects.

Chapter 2 provides a synopsis of the development of the dentin-pulp complex, highlighting its importance, as well as key features of the ectomesenchyme in the development and maintaining healthy teeth. Recent advances and new insights into the biology of the dentin-pulp complex and how they may be exploited to improve dental treatment are highlighted.

Chapter 3 defines dental pain as pain associated with sensory activation of the dentin, whereas pulpal pain is usually associated with an inflammatory reaction of the pulp tissues.

In Chapter 4, the use of local anesthesia is elaborated on, stressing the virtually pain-free treatment and explaining the association with anxious thoughts and misconceptions in young patients.

Chapter 5 stresses that pulp therapy procedures in children and adolescents present dentists with unique challenges, due to the increase of preexisting pain and the complexity of the procedures. For many, the appointment and treatment will be a first-time dental experience. Success is contingent on parental guidance and basic behavior management techniques that promote relaxation and pain control. For children with previous negative experiences, reframing techniques can reestablish a positive dental attitude.

Chapter 6 is a brief overview on caries development and control strategies as well as achieving an accurate diagnosis. This chapter discusses and summarizes the recommendation for the management of initial, moderate, and extensive caries lesions, reaching the outer half of dentin in primary and young permanent teeth.

Chapter 7 provides the readers with reliable, evidence-based data obtained from laboratory studies and clinical trials performed in the last decades in different fields of dentistry related to dental materials, as well as pulp biology and regeneration.

Chapter 8 centers on silver diamine fluoride (SDF) that combines the antibacterial actions of silver with the re-mineralizing effects of fluoride. The combined alkaline stabilizing solution creates a synergistic effect that slows collagen degradation in dentin. Even with the dark staining that characterizes treated lesions, it is an invaluable tool for caries management, especially when traditional restorative care is not a viable first line of treatment.

Chapter 9 explains how determining the accurate status of the pulp of primary and young permanent teeth is a challenging task for any provider treating children and young adults. The younger the child is, the more difficult it is to obtain objective and clear information, since children are considered "poor historians." The goal of this chapter is to provide the clinician with knowledge of currently available tests and evidence-based recommendations, to achieve pulpal diagnosis.

Chapter 10 is a brief overview of caries lesion development and pulp reactions as well as the relationship between the bacterial invasion of dental tissues and the possibility of lesion control. This chapter brings together the existing evidence on conservative treatment, aiming to preserve both tooth vitality and structure. It also summarizes the contemporary approach to the management of deep dentin carious lesions.

Chapter 11 describes bioactive ceramic cements. These types of cement are set with water and have become the standard of care in vital pulp therapy for primary teeth. These bioceramic dental materials are dimensionally stable, strong, and insoluble and so are suitable for pediatric indication, from pulp capping to apexification. Over the past 25 years, they improved enormously in clinical convenience, and the price has diminished.

Chapter 12 focuses on direct pulp capping (DPC) for primary and permanent teeth; it reviews the biological properties of materials used for DPC and factors to be considered before performing DPC. There is now evidence-based dentistry (EBD) research showing that DPC is successful for vital primary and permanent teeth but conflicting evidence on permanent teeth diagnosed as having irreversible pulpitis. Evidence-based dentistry literature is reviewed as well as the techniques for DPC treatment methods.

Chapter 13 discusses pulpotomy, a technique for vital pulp therapy that has been used for decades. The success of this technique varies with the material used as the pulpotomy agent, and all materials used in the last century have both advantages and disadvantages. In the last two decades, the introduction of bioactive calcium silicate cements like MTA and Biodentine has changed the stage, allowing better sealing of the remaining pulp tissue.

Chapter 14 elaborates on pulpectomy, a root canal procedure for primary teeth that is indicated when the radicular pulp exhibits clinical signs of irreversible pulpitis or pulp necrosis, while the roots show minimum or no resorption. This chapter elaborates on the clinical steps of the technique-sensitive pulpectomy treatment, reviews new concepts and technologies, and describes the materials and instruments that are used.

Chapter 15 talks about the use of glass ionomer and other restorative materials. An ideal material should restore the integrity of the tooth structure and the arch, seal the cavity from the oral environment, and prevent recurrent lesions and the spread of infection into the dental pulp. When deep carious lesions are in close proximity to the pulp and extended to multiple surfaces, full coronal coverage is recommended.

Chapter 16 discusses the restoration of the pulp-treated tooth after the completion of the pulp therapy. The types of restorations and their materials are discussed as well as the techniques and tips for using these materials. The chapter aims to provide the clinician with step-by-step guidance as well as options for restorations of pulp in primary teeth.

Chapter 17 discusses endodontic treatment of young permanent immature teeth that differs from that of mature permanent teeth due to their high potential healing properties. The procedure is expected to promote healing and preserve the vitality of the tooth. When other treatment options fail, root canal treatment is carried out. Distinct problems in disinfection and obturation make the treatment very challenging and may also necessitate apexification.

Chapter 18 discusses a variety of post-endodontic treatment options in young anterior and posterior permanent teeth, as well as factors related with long-term success. Endodontically treated young permanent teeth with reduced structural integrity usually require large restorations, which can be challenging for pediatric dentists, due to limited evidence and the lack of an acknowledged standard of care.

1.4 New Developments and Future Directions

Chapter 19 deals with new insights gained by single-cell technologies and focuses on developmental aspects.

Chapter 20 describes the efforts to exploit the regenerative capacity of stem cells in the dental pulp and novel therapeutic approaches that aim to achieve complete regeneration of dental tissues. The authors review fundamental mechanisms of pulp repair and regeneration and discuss novel stem cell-based strategies for dental pulp tissue engineering.

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2 Cellular and Molecular Mechanisms Guiding the Development and Repair of the Dentin–Pulp Complex

Tal Burstyn-Cohen

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2.1 Introduction

Although dentin and pulp of mature teeth differ in composition and physical properties, they share the same developmental origin and constitute a single functional unit. Odontoblasts—the dentin-forming cells—reside within the pulp throughout the lifetime of the tooth, and mesenchymal stem cells within the pulp can differentiate into dentin-laying odontoblasts. Thus, resident cells of the pulp, including immune and pulp stem cells as well as odontoblasts, contribute to dentin repair in adult tissue. Understanding the molecular cues and biological mechanisms that guide development of the dentin-pulp unit and lead to odontoblast differentiation with productive dentin formation may contribute to develop restorative treatments. This chapter will provide an overview of the development of the dentin-pulp

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complex and introduce selected recent advances in understanding the molecular and cellular mechanisms of dentin-pulp development and how they may be harnessed into regenerative dentistry.

2.2 Formation of the Dentin–Pulp Complex

During early embryogenesis, cranial neural crest cells (NCCs) of neuroepithelial origin delaminate and detach from the neural ectoderm, as they undergo an epithelial-to-mesenchymal transition. Their new mesenchymal properties, deriving from ectodermal origin, have gained them a unique name: ectomesenchyme. Neural crest-derived ectomesenchymal cells are important contributors to head and neck development, including dentition. The epithelial-to-mesenchymal transition (EMT) is crucial for tooth development, as ectomesenchymal cells that colonize the mandibular and maxillary arches of the first pharyngeal arch are the progenitors of dentin and pulp. Ectomesenchymal cells undergo morphological and molecular changes, also acquiring a robust migratory potential. As they migrate and populate the pharyngeal arches, ectomesenchymal cells proliferate and differentiate as they respond to local signals within their migratory path. Responding to molecular cues emanating from the adjacent oral ectoderm induces morphological modulations, which are followed by molecular and functional changes transforming NCCs into dental papilla. The dental papilla will further differentiate and give rise to the tooth pulp and surrounding mineralized dentin (Fig. 2.1). With only a basement membrane separating the dental papilla from the overlying ectoderm, both tissues remain in close, physical contact. Successful reciprocal epithelial-mesenchymal interactions between the oral ectoderm and dental papilla layers will provide signals necessary for the coordinated development of these two embryonic layers into mature dental tissues including the pulp, dentin, and enamel (Fig. 2.1).

These reciprocal epithelial-mesenchymal signals instruct molecular and cellular changes, which drive dental development. This process is recognized through a series of morphological changes, which have been classically described as the dental lamina, bud, cap, and the early and late bell stages of tooth development (Fig. 2.1). Another, more recent classification that emphasizes functionality has been used to describe odontogenesis in four phases: initiation, morphogenesis, cell differentiation (cytodifferentiation), and matrix apposition. During *initiation*, the oral ectoderm slightly thickens at the prospective tooth sites, thereby defining the *dental ectoderm*, which marks the location of the future corresponding tooth, still within the continuum of the developing mandibular and maxillary arches. At the *dental lamina* stage, ectodermal cells within these future dental regions undergo rapid and asymmetric proliferation, resulting in their invagination into the underlying ectomesenchyme, defined morphologically as the tooth *bud*. The invaginating dental lamina cells signal to the adjacent ectomesenchymal cells, which respond in aggregation, and signal back to the dental lamina, which expand to form a three-dimensional cap over the aggregated ectomesenchyme, morphologically recognized as the *cap* stage. During the cap stage, first signs of histodifferentiation are observed,

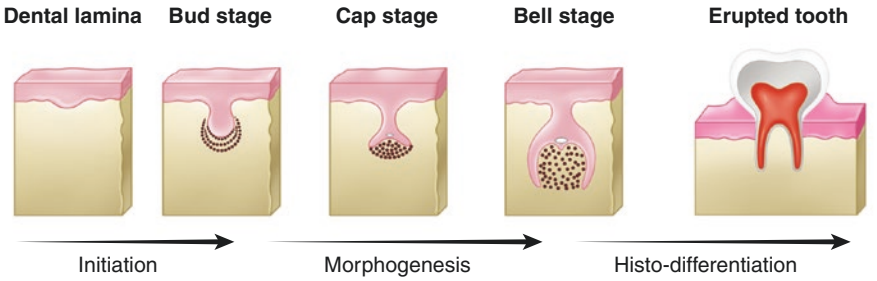

Fig. 2.1 Stages of tooth development.
Oral ectoderm (pink) and neural crest-derived ectomesenchyme (ochre) in the first pharyngeal arch. During the initiation phase, ectoderm thickening marks the site of tooth development. The ectoderm then grows into the ectomesenchymal layer, forming a bud-like structure. The underlying ectomesoderm reacts by cellular condensation (depicted by brown dots) underneath the invaginating ectoderm. The enamel knot (light blue) develops in the center of the bud within the ectodermal tissue and is normally histologically visible at the cap stage. The enamel knot inhibits local ectodermal growth but promotes the growth and elongation of ectodermal tissue located further radially, which results in a bell-shaped tooth bud. The growing front of the ectodermal layer closes on the underlying ectomesoderm, defining the dental papilla (dotted area), which will give rise to odontoblasts and the vital pulp tissue of mature dentition. Cells located at the border of both tissues begin to differentiate: ameloblasts from the inner enamel epithelium (IEE) and odontoblasts from the dental papilla. First signs of mineralization are seen at the bell stage. Finally, in the mature erupted tooth, enamel (white) is the external mineralized tissue, deposited by ameloblasts, which have died and disappeared. Dentin tissue (grey) is formed, surrounding the pulp (red), and is maintained by odontoblasts, which reside within the dental pulp. The gingival tissue (pink) covers and supports the base of the tooth. Dental pulp cells have the capacity to differentiate into odontoblasts and form new dentin. The corresponding functional stages of initiation, morphogenesis, and cyto(histo)-differentiation are aligned below. See text for more details

as the cap forms distinct layers. The innermost layer overlays and defines the underlying ectomesenchyme as the *dental papilla* together with its ensheathing *dental follicle*, which will contribute to the support tissues of the tooth, mainly cementum and periodontal ligament (PDL). The innermost layer of the cap has now differentiated into the *inner enamel epithelium* (IEE) and develops a vital signaling center marking the beginning of crown formation known as the *enamel knot*. Complex signaling pathways within and between the enamel knot and the dental papilla as well as the IEE cells guide cusp formation and hence influence crown morphology. These will be described later in this chapter. Recent research has identified the morphogen Sonic Hedgehog (*Shh*) as a negative regulator of cusp formation [1]. Time lapse imaging of developing tooth buds labeled with fluorescent cell cycle reporters elegantly demonstrates the complex coordination of cellular dynamics and proliferation, which drive tooth formation [2].

Whereas proliferation continues in areas distant from the enamel knot, signals emanating from this organizational center inhibit proliferation of enamel knot and adjacent cells, thereby allowing proliferation of peripheral cells, which transforms

the cap-shaped tooth bud into an elongated structure, which appears histologically as a bell (Fig. 2.1). It is during the *bell stage* that IEE and dental papilla cells terminally differentiate into ameloblasts and odontoblasts, respectively, secreting initial mineralized tissue. This is known functionally as the *matrix apposition* stage. Development and differentiation of both the dental papilla and the prospective enamel continue in a developmental gradient, as the differentiation wave advances to form the full crown of the tooth. Since the onset of root development does not begin until tooth eruption, there is a delay in the development of radicular pulp and the accompanying PDL and cementum. Despite this delay, which may be quite significant (up to 10–15 years for molars), the pulp tissue in mature teeth appears uniform and continuous at the transition between crown and radicular pulp. The subsequent paragraphs will chronologically describe key aspects in pulp development.

2.3 Mesenchymal Condensation and Key Features of the Early Dental Papilla

The first histological evidence marking the future dental papilla within the ectomesenchyme is the cellular condensation, which occurs just under the dental ectoderm. Numerous cellular and molecular mechanisms may lead to cellular condensation. In the mouse an increase in ectomesenchymal cell proliferation localized to the future dental papilla was observed as early as the initiation phase [3]. This increase in ectomesenchymal cell proliferation overlaps with a dynamic co-expression of syndecan and tenascin, which concurs transiently with condensation, as observed in molar teeth of mice. Tenascin and syndecan interact with extracellular membrane proteins and growth factors, which led the authors to propose these proteins regulate local cell-cell interactions, inducing proliferation and thus contributing to local condensation [3]. More recently, a mechano-chemical mechanism was proposed to contribute to mesenchymal condensation [4]. According to the mechano-chemical mechanism, Fgf8 and Sema3f are produced by the dental ectoderm but act differentially on mesenchymal cells. Secreted Fgf8 accumulates at the basement membrane and acts as a morphogen to attract dental papilla cells. Concurrently, the repulsive protein Sema3f is secreted and accumulates at the basement membrane but is later released and acts as a repulsive morphogen. As a result, Fgf8 attracts mesenchymal cells, while Sema3f repels them, resulting in opposing forces being exerted on these cells, leading to their localized condensation. Moreover, mesenchymal cells that underwent tight condensation upregulated the odontogenic transcription factors Pax9, Msx1, Lhx8, as well as BMP4, whereas loosely packed cells did not. These findings identify cell compaction as a mechano-physical mechanism that upregulates odontogenic gene expression within the emerging dental papilla [4]. Additional molecules including transcription factors, morphogens, and cell matrix and membrane proteins have been linked to mesenchymal condensation in tooth development and are mentioned in [5].

At the same time, still within the bud stage, the dental mesenchyme acquires an inductive role, which now drives odontogenesis. This was elegantly demonstrated by Kollar and Biard using heterotypic grafting experiments. When bud-stage dental papilla was co-cultured with ectopic ectodermal tissue isolated from the foot or snout, these heterotypic grafts developed into tooth structures, indicating the molecular driving force for tooth development now resides within the dental mesenchyme [6].

At the cap stage, histodifferentiation occurs within epithelial cells, which turn into the enamel organ. The enamel organ consists of four distinct cell populations: the inner and outer enamel epithelium (IEE, OEE, respectively), the cervical loop (CL), and the stellate reticulum (SR). IEE cells will further differentiate into ameloblasts; the CL cells are stem cell-like cells which will drive root development. The SR and the OEE are transient populations, which provide nutrition and protection to the developing tooth germ. The primary enamel knot (EK) develops at the center of the enamel organ just above the IEE layer and may be considered a fifth cell population due to its distinct cellular organization and key function as a signaling center, which is crucial for shaping the developing tooth. These cell populations develop in defined areas within the tooth bud. The IEE cells are situated immediately adjacent to the underlying dental papilla with which they are known to molecularly interact. The basement membrane (BM) and extracellular matrix separating the dental epithelium and dental papilla allow for accumulation of signaling molecules necessary for the epithelial-mesenchymal cross talk instructing tooth development. The BM will later disintegrate and mark the location of the future dentin-enamel junction.

Thus, tooth bud development is driven by the cross talk between epithelium and ectomesenchyme cells, both tissues acquiring a positional molecular profile and cellular organization, which is postulated to support tooth development. Across the BM, on the mesenchymal side, papilla cells that are located just beneath the IEE will differentiate into odontoblasts, whereas remaining cells will differentiate into other pulp cell populations (see below). Thus, at the cap stage, dental epithelium, papilla, and follicle are clearly distinguished in histological preparations by their morphology and organization, and it is thought that this positional information of both ectodermal and mesenchymal cells is necessary for tooth development. A recent study by Hu et al. has revealed a surprising degree of plasticity within these cells [7]. Dental mesenchyme and epithelium of developing tooth buds at the cap stage were dissected, isolated, and dissociated into single-cell epithelial and mesenchymal suspensions. When these single-cell suspensions were re-associated in vitro, teeth developed. These teeth displayed a characteristic morphology and cellular organization, with differentiated and functional odontoblast and ameloblasts [7], demonstrating the remarkable plasticity of both dental epithelium and papilla at this stage. The ability of both cell types to reorganize and fully reconstruct a tooth bud with a complete and functional enamel organ indicates that despite losing their positional information, epithelial cells have not yet committed to the IEE, OEE, CL, and SR and that mesenchymal cells can still become either papilla or follicle cells. Overall, this and other such experiments suggest that plasticity in situ may be greater than currently appreciated [7–9]. It would be interesting to harness newly

developed techniques such as spatial transcriptomics and single-cell RNA sequencing combined with pseudo time analysis to understand the molecular changes that accompany such cellular reorganizations and underpin tooth development.

It is the dental papilla at this developmental phase that dictates tooth shape and identity. This was shown by Kollar and Biard when molar dental papilla and dental epithelium were isolated at early cap stages from either molar or incisor teeth. The tissues were left intact but recombined such that one tissue was from a molar tooth and the other from an incisor. When papilla and epithelium were taken from tooth germs of the same developmental age (synchronic), the reconstructed tooth shape always matched the original identity of the dental papilla [10]. However, when heterochronic (papilla and epithelium from different developmental ages) reconstructions were made, the instructive potential of the papilla over the epithelium was blurred, with the highest tooth identity (molar versus incisor) attributed to embryonic day 13 papilla, corresponding to the cap stage. These experiments, also supported by additional reconstitution experiments using tissues at different developmental time points and from various locations, indicate that within intact tissues at the cap stage, tooth identity is already determined and that this information is encoded within the dental papilla to form the pulp, cementum, PDL, and alveolar bone, whereas dental ectoderm still exhibits morphogenic plasticity [5, 6, 9–11].

2.4 Odontoblast Differentiation

The majority of the knowledge pertaining to tooth development comes from studies in mice, although single-cell technologies are currently being developed and used to understand both murine and human tooth development. For more on this, the reader is referred to a dedicated chapter on new technologies (See Chap. 19). During the late cap and early bell stages, dental pulp cells residing just under the basement membrane of the dental ectoderm respond to secreted ectodermal signals, which stimulate dental papilla cells to differentiate into pre-odontoblasts and finally into odontoblasts. Thus, it seems that spatial distribution of dental papilla cells at a certain developmental time point, rather than a predetermined fate program, dictates odontoblast fate. This conclusion is also supported by the dissociation experiments described above [7, 9–11]. The molecular reciprocal cross talk between dental epithelium and mesenchyme provides a mechanism, which secures the coordinated development of dental papilla and ectoderm-derived dental tissues, especially toward the deposition of pre-dentin and enamel matrix, which will begin at the late bell stage.

Studies by Ruch et al. that were focused on examining the cell cycle of dental papilla cells showed that dental papilla and pre-odontoblasts undergo about 14–15

mitotic divisions before they become post-mitotic odontoblasts. Lengthening of the cell cycle was recorded as development proceeds from the dental lamina stage to the first post-mitotic odontoblasts [12]. The basement membrane may play an important role in accumulation of numerous extracellular matrix proteins such as fibronectin, tenascin, laminin, hyaluronic acid, and collagens, which may regulate odontoblast differentiation [13]. As pre-odontoblasts develop and approach their terminal differentiation, their mitotic spindle becomes perpendicular to the basement membrane, such that one daughter cell will acquire the position immediately adjacent to the BM and the other daughter cell will be located one cell width below, facing the dental papilla. Only the cells in contact with the BM further undergo terminal differentiation, which is accompanied by cellular elongation, and redistribution of cellular organelles [12, 13]. Terminally differentiated odontoblasts form a terminal web composed of collagen type I and III fibers (von Korff fibers), fibronectin, cytoplasmic filaments, and tight junctions, which function as a barrier sealing off the secretory apical end of the odontoblast from the basal end and the dental papilla. This terminal web barrier therefore allows for directional secretion, accumulation, and mineralization of pre-dentin without being diluted by dental papilla components [13]. The BM degrades as pre-dentin and enamel matrix are secreted. The dentin layer thickens in a process termed appositional growth as odontoblasts secrete newly formed pre-dentin, and the pre-dentin secreted at earlier time points fully mineralizes into dentin. As a result, odontoblasts are pushed and crowded due to the forming crown concave curvature into the dental pulp. Mature odontoblasts may remain viable for decades; however, their secretory capacity decreases. The initial "mantle" dentin secreted is less organized as odontoblast still undergo maturation and their secretory organelles mature, allowing for continuous and organized apposition of pre-dentin, which mineralizes into primary dentin. Secondary dentin apposition is slower and initiates with root formation. The transition between primary and secondary dentinogenesis is also reflected by odontoblast morphology, specifically the reduction in the secretory machinery by autophagy, reduction in cell size, and overall flattening, which has been described for human-aged odontoblasts [14].

Terminal differentiation of odontoblasts is also regulated by the IEE and the BM, which serves as a matrix onto which numerous cell adhesion and extracellular matrix signaling proteins (such as fibronectin, tenascin, laminin, and chondroitin sulphate) and growth factors (IGF-1, BMPs and TGFβ proteins) accumulate [13].

Differentiating radicular odontoblasts can be detected in human teeth during root elongation. The morphological differences between mature pulp and the still developing dental papilla are also visible in an incisor tooth that had erupted but is still growing its root (Fig. 2.2).

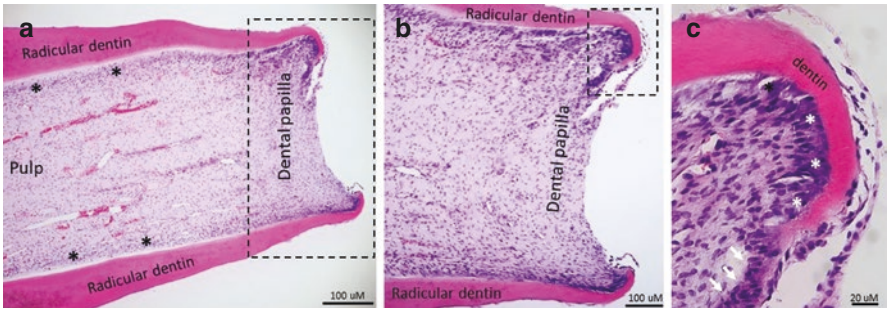

Fig. 2.2 Pulp and dental papilla in a developing tooth.
(**a**) A longitudinal view of the apical aspect of an incisor tooth extracted from a 2-year-old patient. The root is still growing, radicular dentin is indicated. While the pulp toward the crown (to the left) is fully developed with visible vasculature, the apical aspect of the root is still developing. Fully differentiated dentin-producing odontoblasts reside in the pulp periphery (black asterisks). The dental papilla cells are located at the apical aspect of the tooth, to the right (boxed area). The boxed area is magnified in B.
(**b**) The apical, developing aspect of the root. This region still contains undifferentiated dental papilla cells. The area marked by the rectangle is magnified in C.
(**c**) New dentin deposited by young odontoblasts (white asterisks) near the cervical loop. The dental papilla cells undergoing odontoblast differentiation are located more centrally (white arrows). Hematoxylin and Eosin staining. *These images are courtesy of Prof. Anna Fuks*

2.5 Dentin Regeneration and Repair

Primary and secondary dentin are physiological dentins, as they are naturally formed throughout the life of the vital tooth. Primary dentin is formed prior to tooth eruption, while secondary dentin deposition commences after tooth eruption. Adult teeth have the capacity to regenerate dentin and form tertiary dentin in response to injury, disease, or other physiological insult. Tertiary dentin is deposited in response to a range of stimuli and reflects the important role of the dentin-pulp complex as the first line of defense against pathogens, including cariogenic bacteria that have entered dentin tissue (illustrated in Figs. 2.3 and 2.4).

The different types of injury and impact on the tooth instigate distinct reparative processes. In case of a relatively subtle stimuli such as shallow dentin caries, gentle trauma, or operative procedure, *reactionary dentin* is formed by the viable odontoblasts, which deposit pre-dentin. Such dentin appears rather similar in structure to the physiological dentin, featuring relatively organized dentinal tubuli, which are often continuous to those in the physiological dentin (Fig. 2.5). Sub-odontoblastic Hoëhl cells present in the subodontoblastic layer may also differentiate into odontoblasts to secrete pre-dentin. However, when odontoblasts are more massively affected by severe trauma, invasive carious lesions, or noxious agents, mesenchymal stem cells are recruited from the deeper layers of the pulp and differentiate into odontoblasts in response to odontogenic cues. Such *reparative* dentin is formed at higher pace and is characteristically disorganized [13, 15].

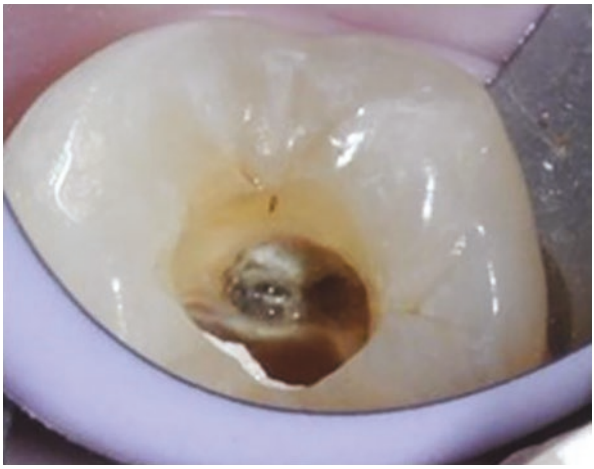

Fig. 2.3 Occlusal view into decaying dentin. A clinical image before root canal obturation. The infected pulp has been removed, exposing carious dentin (gray area). View through an access hole that has been made in the crown enamel. *This image is courtesy of Dr. Sharonit Sahar-Helft*

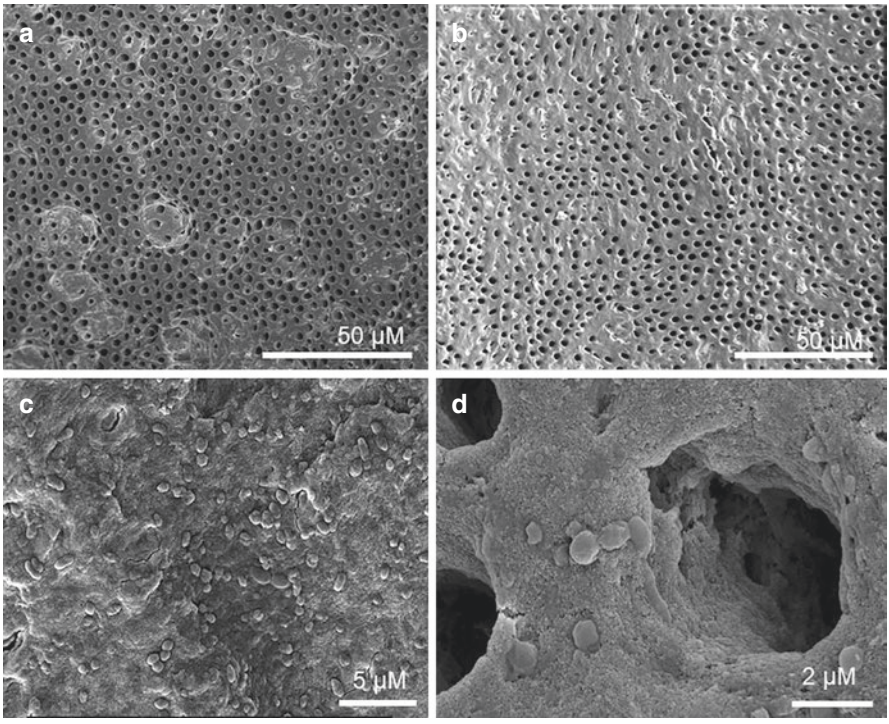

Fig. 2.4 The ultrastructure of dentin as visualized by scanning electron microscopy (SEM). (**a**) SEM micrograph of a specimen showing healthy dentin with open dentinal tubuli. The globular structures represent a globular (calcospherie) mineralization of dentin.
(**b**) In this specimen, most dentinal tubuli are open; some are sclerotic. Sclerotic tubuli may indicate the odontoblasts processes that reside within the tubuli and maintain them have died.
(**c**) Dentin with a bacterial biofilm. Bacteria appear as small round balls, and the dentinal tubuli have been covered by the bacterial biofilm.
(**d**) A larger view into a dentinal tubuli with several bacteria on the dentin surface. *This image is courtesy of Dr. Sharonit Sahar-Helft*

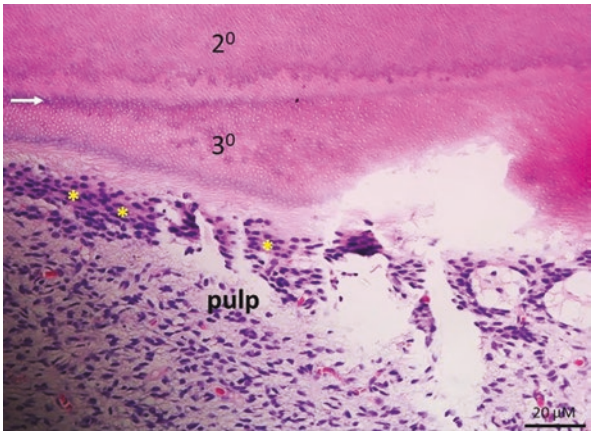

Fig. 2.5 Reactionary dentin.
Reactionary (tertiary, 3°) dentin is produced in reaction to mild trauma or stimuli and is confined to the affected area. Physiological (secondary, 2°) dentin is located more peripherally. The white arrow points to the line separating secondary and tertiary dentin. Dentinal tubuli appear as organized parallel white lines in the physiological dentin and are less organized in the reactionary dentin. The odontoblasts that have produced the reactionary dentin are marked by yellow asterisks. Some artifacts in preparation are seen as white regions devoid of organic matter. Hematoxylin and Eosin staining. *This image is courtesy of Prof. Anna Fuks*

Much research is focused on revealing and understanding the molecules and mechanisms, which drive pulp stem cells to differentiate into odontoblasts, as this would potentially allow the exploitation of the pulp stem cell pool for regenerative purposes in restoration of dental pulp or dentin and beyond. Indeed, pulp regenerative therapies were previously reported for single-rooted teeth and recently for multi-rooted teeth [16].

Understanding the molecular pathways leading to odontogenesis and dentinogenesis would advance the development of therapeutic dentin restoration. Neves et al. recently reported successful dentine formation and restoration following manipulation of the Wnt signaling pathway [17]. In a mouse molar tooth damage model involving pulp exposure, delivery of the small molecule inhibitor for Glycogen synthase kinase-3 (GSK-3) activated Wnt signaling within the dental pulp, which promoted the formation of reparative-like dentin [17]. Further investigations into how to best mimic and promote the natural process of reparative dentin formation are expected to contribute to dentin restoration and protection of injured or inflamed pulp.

Insights into human odontoblast differentiation are mostly gained by ex vivo experimentation, allowing for structural, molecular, biochemical, and gene expression analysis. For example, third molar human dental pulp cells from 14 to 16-year-old donors were isolated and differentiated ex vivo into odontoblast-like polarized cells, which presented with many known in vivo odontoblastic cellular and morphological features. Differentiated odontoblast-like cells contained secretory vesicles, presented with odontoblastic processes, generated gap and desmosome-like

junctions, and secreted dense bundles of extracellular matrix and collagens. Moreover, needle like crystals with the composition and structure of hydroxyapatite (HAP) were observed, as well as transcripts encoding the dentin matrix protein DSPP [18].

Given that dental pulp stem cells share many similarities with mesenchymal stem cells from other locations, including bone marrow mesenchymal stem cells [19], their full therapeutic potential is yet to be discovered. Molecules of prominent morphogen and growth factor signaling pathways play a role in the maintenance of pulp stem cells and their differentiation to functional odontoblasts. Members of the BMP (Bone Morphogenetic Proteins), Wnt (Wingless and Int-1), and Shh (Sonic Hedgehog) pathways have been identified to regulate dental stem cell biology [15, 18–21]. IGF (insulin growth factor)-1 and IGF-2, FGFs (fibroblast growth factor), PDGF (platelet-derived growth factor), VEGF (vascular endothelial growth factor) have all been implicated in these processes [12, 13, 21, 22]. Some of these molecules are constituents of the dentin, embedded within the dentin matrix during dentinogenesis and may be released or exposed upon tooth decay or insult [23]. Immune and inflammatory events were also shown to be upregulated and participate in the complex processes, leading to odontoblast differentiation and dentin repair, described below.

2.6 The Role of Inflammation in Dentin Biology

Because regenerative dentin is produced in response to injury or infectious stimuli, the immune system is also activated. Similar to other body tissues, sentinel immune cells reside within the pulp under steady-state conditions and are important for effective immune surveillance and for maintaining tissue homeostasis, including the regulation of cell proliferation and removal of apoptotic cells [24, 25].

Numerous pulp cells participate in the inflammatory response by secreting cytokines or otherwise responding to danger signals upon injury [13, 15, 21, 26]. These cytokines not only recruit immune cells as part of an inflammatory process but also signal onto dental pulp stem cells and odontoblasts, which express cytokine receptors [25, 27–30]. Neves et al. have recently reported that upon injury to dentin, pulp-resident macrophages accumulate at the injury site and remain [31]. Moreover, ablation of macrophages delayed Wnt-induced modulation of pulp stem cells and their engagement in reparative dentin formation [31].

However, lessons from numerous inflammatory models have shown that controlling the magnitude and duration of inflammation is crucial for tipping between a potentially destructive or reparative environment [32]. This is also true for inflammation within the dentin-pulp complex, reviewed in [33]. Regulated inflammation serves as a defense mechanism against infection and injury and supports tissue repair, while chronic or acute inflammation may promote disease. A recent transcriptomic study revealed the heterogeneity of immune cells present in the pulp of both mouse and human pulp [34] and bacterial components are also recognized by other cells of the pulp including fibroblasts and stem cells [35, 36] in addition to odontoblasts, as mentioned above.

2.7 Concluding Remarks

This chapter highlighted the basic cellular and molecular mechanisms guiding the development of the dentin-pulp complex. Significant dentinogenesis takes place postnatally, but all forms of dentinogenesis are essentially a developmental process. The challenges aiming at controlling dentin repair for better oral and tooth health rely on understanding the molecular mechanisms as well as the numerous cell types involved and how to harness their complex biology to improve dental treatment.

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Dental Pain, Mechanism of Action

3

Yaron Haviv, Shirley Leibovitz, and Yair Sharav

Contents

Pain according to the recent definition of the IASP (International Association for the Study of Pain) is "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" [1]. It can be acute or chronic and contains a complex orchestra of physiological and psychological mechanisms.

Dental pain is a very common type of pain. The term dental pain refers to dentinal pain associated with sensory activation of the dentine and pulpal pain associated usually with inflammatory reaction of the pulp tissue.

Dentinal pain, derived from stimulation of the dentine, has unique features; any sensory stimulation, such as mechanical, thermal, or chemical, results in pain. No sensations such as touch, cold, or warm are reported under these stimulations. Furthermore, the mechanisms of dentinal pain conduction are not explained by direct nerve conduction for reasons discussed below. Dentinal pain results from exposure of the dental tissue usually by carious lesions or due to trauma. Pain derived from the pulp is unique in the sense that the pulp tissue is confined by dental hard tissue that does not allow for inflammatory tissue swelling or expansion,

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resulting in excruciating pain. Pulp inflammation is usually the result of infection mostly by carious lesions invading the pulp or occasionally due to migraine-like neurovascular central mechanisms. We also refer to a pre-pain phenomenon, another feature of dental pain.

3.1 Dentinal Pain

Dentin hypersensitivity is one of the most common complaints of patients in the dental clinic [2]. There have been many reviews regarding the mechanisms of sensitivity and/or pain in the dentine of mammalian teeth [3–8]. A recent narrative review relates to some of the recent research that expanded our knowledge and possible new theories for dentinal sensitivity. It suggests a relation among odontoblasts and dental afferent neurons that takes place by the release of several mediators, which are involved on the transduction of dentinal pain (Fig. 3.1) [9].

When examining how far nerve fibers originating in the pulp extend into the dentine, microscopic analyses revealed that the nerves reach about half as far as the odontoblastic processes, and never get all the way to the dentino-enamel junction

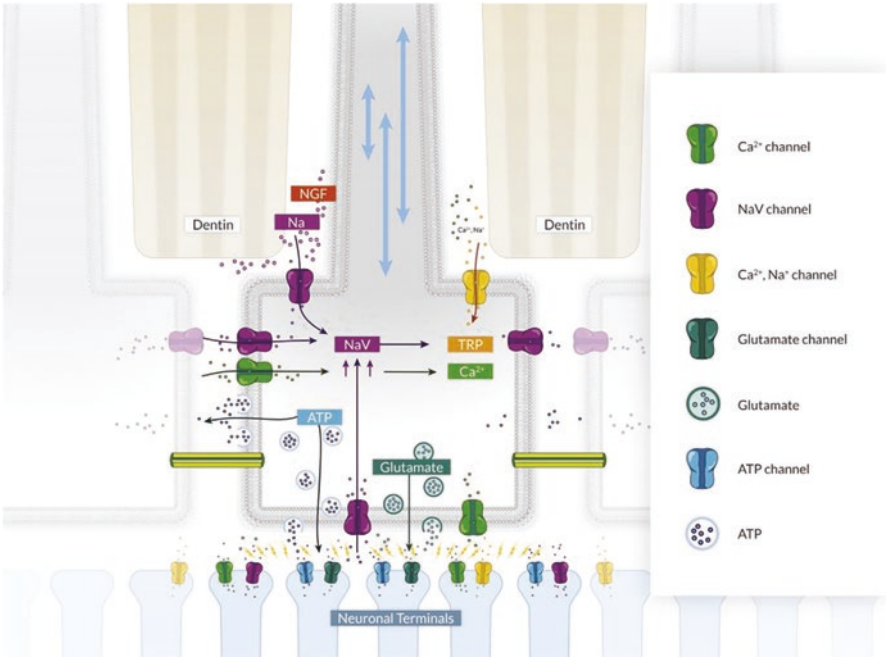

Fig. 3.1 The cross talk between odontoblasts and axons may take place by the release of mediators. About 10% of the dental pulp afferent neurons express TRPV1, which was upregulated by caries and caries by-products. These results suggest that odontoblasts and dental afferent neurons are involved in the transduction of dentinal pain (Aminoshariae and Kulild 2021, by permission) [9]

[5, 10]. It has been suggested that the odontoblast itself may be able to act as a receptor for sensory input within the dentine [11]. A study based on immunohistochemistry showed the presence of the Transient Receptor Potential Vanilloid Subfamily Member 1 (TRPV1) channel on odontoblast membranes, suggesting that these cells can respond to heat or other noxious stimuli [12].

Furthermore, the evidence of gap junctions between neurons and odontoblasts is inconclusive [13, 14].

When studying dentinal pain, experiments have shown that stimuli such as drying with absorbent paper or blowing air, physical trauma (e.g., cutting, scratching, probing), and changes in osmotic pressure, temperature, or pH cause pain. On the other hand, placement of known algesic solutions (which cause pain when applied to the base of a skin blister [15]), e.g., potassium chloride, acetylcholine, 5-hydroxytryptamine (5-HT), bradykinin, and histamine, on exposed dentine did not cause pain [4, 16]. The lack of nerves within the dentine and the absence of pain following the application of neuroactive chemicals led to alternative hypotheses about the mechanisms of dentinal pain, including the hydrodynamic theory by Brannstrom [17]. Brannstrom proposed that the movement of fluid within the dentinal tubules is able to alter the structure of nociceptive fibers in the pulp, thereby activating mechanoreceptors and causing the transmission of a pain signal. Evidence supports Brannstrom's hypothesis, whereas other proposals, e.g., the neural theory and odontoblastic transduction theory, have not been substantiated yet [14]. By behaving as a passive hydraulic connection between the stimulated area and pressure-sensitive neuronal terminals in the pulp, the dentinal tubules transfer the signal of the existence of a noxious stimulus. These pressure-sensitive nerve cells have group A fibers that are much more sensitive to outward fluid flow than inward flow in the dentinal tubules [18]. The hydrodynamic theory was supported by findings suggesting the involvement of the transient receptor potential (TRP) channel family, a class of mechanosensitive ion channels expressed in the sensory system of the teeth [19, 20]. An extensive review by Magloire et al. discusses facts and hypotheses associated with dental pain and the odontoblasts [7].

Thus, for example, while the hydrodynamic theory still keeps valid, there are some concerns regarding the low threshold stimuli producing dentinal pain. This problem is addressed by Fried et al. [21], suggesting that pain is activated by low-threshold mechanoreceptors having pain-provoking CNS connectivity. Dental pain, including dentinal but more specifically pulpal pain, was discussed in a recent article referring to the new International Classification of Orofacial Pain (ICOP) and is of benefit for both clinicians and researchers [22].

3.2 Pulpal Pain

The overriding consensus is that pain in the pulp is related to inflammation and its mediators including cholinergic and adrenergic neurotransmitters, prostaglandins, and cyclic adenosine monophosphate (cAMP) [23, 24]. Molecules such as prostaglandins (especially PGE2), bradykinin, and serotonin are able to activate neurons

in the pulp. A study on bovine teeth showed that bradykinin-evoked calcitonin gene-related peptide (CGRP) release is increased by PGE2 [25]. A recent study demonstrated upregulation of Toll-like Receptor 2 in dental primary afferents following pulp injury [26]. Neurogenic inflammation occurs when trigeminal afferents are stimulated antidromically and release vasoactive neuropeptides, including CGRP, which play a central role in the initiation of neurovascular type headaches [27]. Analysis of human dental pulp revealed significantly greater expression of CGRP, SP, and VIP, in permanent teeth relative to deciduous counterparts [28, 29].

This may explain the lack of children in reports of neurovascular vascular orofacial pain (NVOP), a pulpal neurogenic inflammatory response in reaction to a migraine-like antidromic activation [30, 31]. The onset and regulation of neurogenic inflammation in the pulp are thought to be related to bradykinin released during inflammation. Furthermore, as caries progresses, there are significant elevations in the neuropeptide Substance P (SP) integral to nociception. Interestingly, specimens from painful teeth had higher levels of SP than those from asymptomatic teeth [32]. SP affects the microvasculature both directly and indirectly, by interacting with smooth muscle cells and causing histamine release, respectively, and alters its permeability. Edema formation (modulated by nitric oxide [33]) and the ensuing extravasation of plasma proteins are caused by SP and are essential to its pro-inflammatory effects [34] [35]. The altered pulpal vasculature lowers oxygen tension and the impaired microcirculation, together with the inflammation, increase the intra-pulpal pressure. The pressure changes are uniquely painful in the teeth because the nerve tissue is surrounded by dental hard tissues [36]. Higher levels of endotoxin were found in teeth with exudation, whereas elevated levels of PGE_2 were detected in teeth sensitive to percussion and palpation [37]. The expression levels of tumor necrosis factor alpha (TNF alpha) in teeth with irreversible pulpitis correlate with the severity of pain [38]. Glutamate receptors and vesicular glutamate transporters (VGLUT) found in both the pulp and trigeminal ganglion support the notion that a distinct glutamate signaling mechanism is involved in dental pain transmission and processing [39]. While it is clear that inflammation is involved in pulpal pain, the interaction of its mediators and specific nerve fibers in the pulp is still being investigated. In contrast to the C-fibers, pulpal A-fibers seem to be unaffected by most inflammatory mediators [6]. However, leukotriene B4 (LTB4), a hyperalgesic factor with prolonged effects, sensitizes A-delta fibers [40]. Studies have shown that C-type nociceptors are essential to the transmission of pain signals from inflamed pulp tissue [24]. Interestingly, the pulp may be able to detect sensations that are not painful, in particular following electric stimulation, [41] and the transmission of these sensations may be via specific afferent nerves [42]. Based on results of experiments using non-painful temporal and spatial summation, it seems that “pre-pain” and painful sensations caused by electrical stimulation are evoked by A-fibers [43, 44]. The hypothesis that there are two discrete types of afferent nerves in the pulp is supported by Narhi et al. They noted that many of the myelinated fibers in the pulp are of the A-β type, which may be responsible for the pre-pain sensation evoked by electrical stimulation [18]. An interesting observation is that teeth with open apices are frequently unresponsive to electric stimulation [45].

Considering that neuronal tissue is present at the time of eruption [46] and that masseteric reflex activity occurs when these teeth are electrically stimulated [45], it seems that segmental reflex connections are established prior to full functionality of the cortical sensory projections [45].

Alterations in the trigeminal nuclei are among the physiological and chemical central nervous system reactions to inflammation of the pulp. The changes have been recorded in: mechanoreceptive fields; the response properties as well as NMDA receptor mechanisms [47–50]. This chapter focuses on the mechanisms of dentinal and pulpal pain; however, this is only the first step in the pain journey from teeth to the cortex. Briefly, the sensory innervation of the teeth arises through the mandibular and maxillary branches of the fifth trigeminal cranial nerve to the gasserian ganglion and from there through the subnucleus caudalis of the trigeminal nucleus located in in the midbrain, through the ventral trigeminothalamic tract to the thalamus and finally to the cortex [51].

Pain expression stems from a complex interaction of many variables, resulting in an unpleasant sensory and emotional experience and not just a result of a noxious stimulus. Pain management is therefore associated with removing the cause of the noxious stimulus as well as alleviating fear and anxiety and addressing the personal characteristics of each patient.

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Assessment and Management of Pain in Pediatric Dentistry

4

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Contents

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4.1 Local Anesthesia in Pediatric Dentistry

Pain control is a central aspect of children's cooperation during dental treatment and is thus a particularly important component of pediatric dentistry. Fear-related behavior has long been recognized as the most difficult aspect of patient management and can be a barrier to good care.

Children who experience early painful procedures are likely to avoid dental treatment throughout their lives. The most common sources of dental fear are the fear of pain and fear of "the needle" and "the injection."

Local anesthesia enables virtually pain-free treatment yet is associated with anxious thoughts and misconceptions in young patients. Administering local anesthetic injection may provoke anxiety not only in patients but also in dentists. In a survey study, dentists reported a high level of stress when delivering local anesthesia to anxious children, regardless of the responders' years of experience, whether they were pediatric dentistry specialists, their age, or sex [1].

The ideal anesthetic technique includes a painless procedure, either during the delivery of the local anesthesia or during the operative procedure. According to Klingberg et al., current evidence is insufficient in support of any pharmacologic agent or injection technique as being superior to others [2].

4.2 Topical Anesthesia

The goal for topical anesthesia is to blunt the effect of the administration of local anesthesia. Topical anesthesia minimizes painful stimuli or dulls the effect of the procedure. A painful stimulus can be either the penetration of the needle or the delivery of the local anesthetic solution. A topical anesthetic reduces the discomfort that may be associated with insertion of the needle before injection of the local anesthetic.

Topical anesthesia can be administered as gels, cream, ointment, liquid, sprays, or lotions. Benzocaine, which is one of the most common topical anesthetics, can be purchased over the counter or with prescription [3].

The mucosa at the site of the intended needle insertion should be dried, and a small amount of topical anesthetic agent is then applied to the tissue with a cotton swab. The effect is achieved within about 30 s, although keeping it in the place for 2–3 min may provide the best results [4].

If dental treatment is needed in a child under the age of 2, topical anesthesia should be avoided due to the risk of developing benzocaine-induced methemoglobinemia (BIM) [5].

4.3 Needle Selection

Needle selection should allow profound local anesthesia and adequate aspiration. Needle gauges range from size 23 to 30. Needles with lower-gauge numbers have larger inner diameters and provide less deflection as the needle passes through soft tissues and more reliable aspiration. The depth of insertion varies not only by injection technique but also by the age and size of the patient. Dental needles are available in three lengths: long (32 millimeters [mm]), short (20 mm), and ultrashort (10 mm). Most needle fractures occur during the administration of inferior alveolar nerve blocks with 30-gauge needles. A needle can break upon insertion to the hub, when the needle is weakened due to its bending before insertion into the soft tissues, or by patient movement after the insertion [6].

A short (20 mm) or a long (32 mm), 30- or 27-gauge needle may be used for most intraoral injections in children, including mandibular blocks (Fig. 4.1).

According to Kupietzky and Schwartz [7], short needles should be used for all techniques (excluding intraligamentary injections), regardless of age and the type of injection.

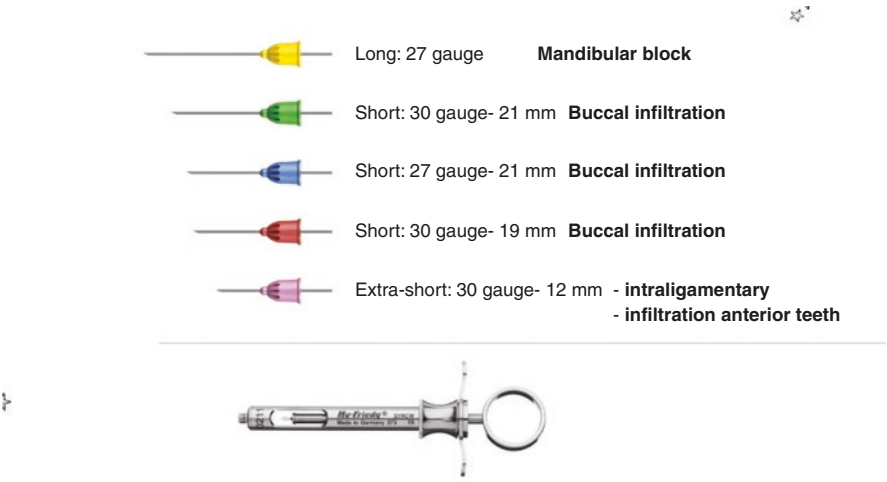

Fig. 4.1 Needles

4.4 Injection Rate

There is no consensus regarding the optimal rate of delivery of local anesthesia, but most authors and clinical practice guidelines have recommended a slow rate. According to Melamed, slow injection is defined ideally as the deposition of 1 mL of local anesthetic solution in not less than 60 s. Therefore, a full 1.8-mL cartridge requires about 2 min to be deposited [8]. However, Kupietzky et al. do not recommend a prolonged injection procedure [7]. The authors of this chapter support Melamed's recommendation as a means of reducing pain.

4.5 Techniques of Local Anesthesia

The most common techniques for local anesthesia in children are conventional injections and computerized local anesthesia.

4.6 Conventional Local Anesthesia

4.6.1 Supraperiosteal Technique: Local Infiltration

This technique is indicated for anesthetizing maxillary teeth (primary and permanent) and mandibular anterior teeth. The use of this technique for mandibular molars is controversial. According to Oulis et al. and Sharaf et al. [9, 10], infiltration of primary mandibular teeth is appropriate for restorative treatment but does not provide sufficient anesthesia for pulp treatment and extractions. The recommended needles for this technique are short 30-gauge for posterior teeth and extra-short for anterior teeth.

4.6.2 Palatal tissue's Anesthesia: Papillary-Interdental Anesthesia

After anesthetizing the buccal aspect of the tooth (Fig. 4.2), the child is asked to bite a cotton roll, and the needle is penetrated into the papilla parallel to the occlusal plane; the solution is injected until the blenching of the palatal aspect is achieved.

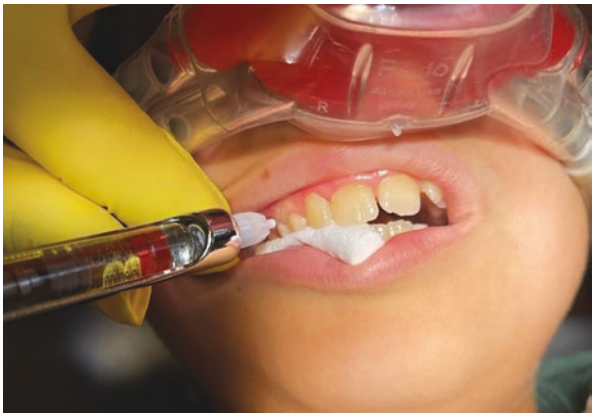

Fig. 4.2 Palatal tissue's anesthesia

4.7 Inferior Alveolar Nerve Block (IANB)

This technique is recommended when multiple teeth will be treated in the mandibula and when a deep operative or surgical procedure will be undertaken for mandibular primary and permanent molars. An advantage of this technique is that with the penetration of a single needle, we anesthetize the buccal and lingual aspects.

According to Melamed [8], the IANB, commonly (but inaccurately) referred to as the mandibular nerve block, is the second most frequently used technique (after infiltration) and possibly the most important injection technique in dentistry. Unfortunately, this technique is also the most frustrating, as evident by the highest proportion of clinical failures, even when administered properly. A suggested reason for failure is inadequate mouth opening. In this situation, the inferior alveolar nerve, which descends, is relaxed a distance from the medial wall of the ramus; this results in inadequate anesthesia. In contrast, when the mouth opening is adequate, the nerve is flushed against the medial wall of the ramus and at the target area. (Failure of inferior alveolar nerve block: exploring the alternatives [11]). Therefore, the use of a mouth prop is recommended to achieve adequate mouth opening during the injection time.

As the soft tissues will remain anesthetized up to 180 min, children could bite their lips and tongue.

The IANB should be complemented with a long buccal nerve block in order to anesthetize the buccal soft tissues and the periosteum adjacent to the mandibular molars. A separate injection for buccal anesthesia is not always necessary, as in young children, the ramus is narrower. Therefore, after mandibular block anesthesia, the buccal tissue usually becomes anesthetized; this is probably due to the enervation of the buccal mucosa by nerve fibers that emanate from the mental foramen [7].

4.8 Computer-Controlled Local Anesthetic Delivery

Computer-controlled local anesthetic delivery (C-CLAD) is a method used to reduce patient pain during local anesthesia. The computerized device enables controlling the injection speed and the pressure induced during delivery. This technology has enabled more comfortable administration of potentially painful injections.

The first C-CLAD device, The Wand, was introduced in 1997. C-CLAD systems represent substantial change in the manner in which local anesthetic injections are administered. Accordingly, the operator can focus attention on needle positioning and insertion, while the motor in the device administers the drug at a reprogrammed rate of flow. It is likely that greater ergonomic control coupled with fixed flow rates is responsible for the improved injection experience demonstrated in many clinical studies conducted with C-CLAD devices in dentistry [8].

At present, several C-CLAD systems are available on the market: The Wand STA Single Tooth Anesthesia System (Milestone Scientific Inc., Livingston, New Jersey), Calaject (Aseptico Inc., Woodinville, Washington), and EZ Flow (Denterprise International Inc., Ormond Beach, Florida) are marketed in the USA, DentaPen and QuickSleeper are marketed in Europe, and similar devices, such as the Anaeject, are marketed in Japan.

C-CLAD devices enable comfortable administration of local anesthetics in virtually all areas of the oral cavity. This is of greatest importance in the palate, where the level of patient discomfort can be considerable. The nasopalatine nerve block, as well as other palatal injections (e.g., AMSA, the palatal approach anterior superior alveolar), can be administered atraumatically. Presumably, any injection technique with even a remote possibility of being uncomfortable for a patient can be delivered more comfortably with a C-CLAD device.

4.9 Behavior Management During Local Anesthesia

The authors of a Cochrane systematic review published in 2020 concluded that due to variations in methodology and the nature/timing of outcome measures, the evidence is insufficient as to the best interventions for increasing acceptance of local anesthesia in children [12]. This study [12] examined several behavior management techniques before, during, and after administration of local anesthesia. These included the use of equipment intervention (audiovisual aids such as audiovisual glasses, television, music), intervention by the dentist, video modeling, and hypnosis. The authors of that study could not demonstrate a superior technique.

The authors of this chapter recommend the use of traditional behavior management techniques that include Tell-Show-Do and distraction, with emphasis on the use of modern equipment for distraction such as screens (television, audiovisual glasses, mobile phone, and others).

There is no agreement in the literature regarding a preferable jaw for the first treatment and whether the anesthetic technique affects a child's behavior at the following dental visit. Ram et al. concluded that more adverse reactions were observed in children following mandibular block than maxillary infiltration, yet this did not result in increased opposition to attend a subsequent dental appointment [13].

During administration of local anesthesia, the dentist should explain to the child what is going to happen, that only the tooth is going to sleep (the child will not be going to sleep) and that a tickling or funny sensation will be felt in the area.

The technique of local anesthetic administration is an important consideration in pediatric patient behavior guidance. Age-appropriate nonthreatening terminology, distraction, topical anesthetics, proper injection technique, and pharmacologic management can contribute to a positive experience during administration of local anesthesia. In pediatric dentistry, the dental professional should be aware of proper dosage (based on body weight) to minimize the chance of toxicity and the prolonged duration of anesthesia, which can lead to self-inflicted tongue or soft-tissue trauma [6].

One study found that the region of local anesthetic injection did not affect children's behavior during and immediately after dental treatment [13].

Testing the effectiveness of local anesthesia is imperative. The dental procedure should never start before ensuring that the relevant area is completely anesthetized. Pain is a subjective feeling; if a child complains about pain, we should always believe the child's feeling and check the anesthesia.

4.10 Materials and Solutions

The most common solutions used in pediatric dentistry are lidocaine, articaine, and mepivacaine (Table 4.1).

Table 4.1 Materials and solutions

Dose	Duration of anesthesia
Lidocaine 2% Epinephrine 1:100.000 Max dose 4.4 mg/kg Cartridge contains 36 mg	**Pulpal: 60 min** Soft tissue: 3–5 h
Mepivacaine 3% *No vasoconstrictor* Max dose 4.4 mg/kg Cartridge contains 54 mg	**Pulpal: 20–40 min** Soft tissue: 2–3 h
Articaine 4% Epinephrine 1:100.000 1:200.000 Max dose 5 mg/kg (5–12 years old) 7 mg/kg >12 years old Cartridge contains 72 mg	**Pulpal: 60–90 min** Soft tissue: 3–8 h

4.11 Side Effects and Complications

A number of potential complications are associated with the administration of local anesthetics. These complications can be classified as local—in the region of the injection—and systemic [8].

4.12 Toxicity

Young children are more likely to experience toxic reactions because of their lower body weight. The potential for toxic reaction increases when local anesthesia is used in conjunction with sedation medication.

Local anesthetic overdose results in excitation, followed by depression of the central nerve system and to a lesser extent of the cardiovascular system (CVS). Overdose reactions and allergy are important topics that should be considered when anesthetizing a child. When administered properly and in therapeutic dosages, local anesthetics cause little or no clinical evidence of depressing the central nervous system (CNS) or the CVS. However, signs and symptoms of selective CNS and CVS depression develop with increased blood levels in the cerebral circulation or myocardium. Early subjective symptoms of CNS toxicity include dizziness, anxiety, and confusion and may be followed by diplopia tinnitus, drowsiness, and tingling. Objective signs of CNS toxicity include muscle twitching, tremors, talkativeness, slow speech, and shivering followed by overt seizure activity. Unconsciousness and respiratory arrest may occur. Local anesthetic toxicity should be avoided, by following proper injection technique and calculation of maximum recommended dosages based on the child's weight.

4.13 Allergy

Allergies to solutions used in local anesthesia can manifest as urticaria, dermatitis, angioedema, fever, photosensitivity, and anaphylaxis. Patients may exhibit a reaction to the bisulfite preservative added to the anesthetic containing epinephrine. The risk of allergy to local anesthetics in pediatric patients is overestimated. In addition to negative skin tests, a subcutaneous challenge with the particular local anesthetic should be performed. Patients with positive skin tests should undergo a skin test and challenge with an unrelated local anesthetic, in search of an alternative drug. This approach will minimize the number of children who are wrongly denied the benefits of LA use in future procedures [14].

4.14 Trauma to Soft Tissue

The duration of the soft-tissue anesthesia is greater than the pulpal anesthesia, and the effect persists for hours after the injection. Self-induced soft-tissue injuries following accidental biting or chewing of the lip, the tongue, or the cheek are reported as complications of the administration of local anesthesia [8]. As no pain is felt, a child may bite soft tissues out of curiosity associated with the unfamiliar sensation of numbness or inadvertently during postoperative eating or sleeping. These injuries commonly present with localized swelling, edema, and pain. Most lesions are self-limiting and heal without complications; however, swelling may cause anxiety in the parents, and they might wonder if the accident occurred during the treatment [15].

The sensation of the numbed tissues should be emphasized to the parents, as well as the need to avoid biting and scratching the anesthetized tissues. Ram et al. demonstrated that licking an ice popsicle after dental treatment with local anesthesia reduces the feeling of discomfort and the biting of soft tissue and self-mutilation [16, 17].

In summary, in deciding to deliver local anesthesia to a child, we should adopt a holistic approach that considers the child's age, medical condition, personality, dental experience and family, and the treatment required to tailor the optimal technique and solution to the child.

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Behavioral Approaches as an Adjunct for Pulp Therapy

5

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5.1 Introduction

Dentistry is one of the only areas in healthcare where surgical procedures are routinely performed on children with minimal or no sedation. Behavior management or guidance is "the means by which the dental team effectively and efficiently performs treatment for a child and at the same time instills a positive dental attitude" [1]. Behavior guidance is a spectrum that includes nonpharmacologic and pharmacologic techniques, often in dynamic interplay as shown in Fig. 5.1. Early publications on behavior guidance were primarily anecdotal in nature, but the field has evolved to include evidence-based techniques.

Behavior guidance for pulp therapy merits specific focus. Pulp therapy is indicated for extensive carious lesions or dental traumatic injuries, both conditions associated with pain. Uncontrolled pain increases dental anxiety and unmanaged anxiety upregulates pain creating a vicious cycle. Pain or trauma may prompt a first dental visit for a child who has not as yet established a dental home, which is an unfavorable introduction to the dental setting (Figs. 5.2 and 5.3). In a university-based clinic, Agostini found that one quarter of children had an emergency dental visit as a first visit [2]. Children may be referred for pulp therapy from a general dentist or dentist less skilled at treating children and may have already had a negative prior dental visit. Finally, pulp therapy procedures are more technically challenging than routine operative dentistry and may require lengthier visits, less tolerance for movement, and the need for repeat visits. In certain clinical situations, profound dental anesthesia may not be achievable. The benefits of preserving the dentition and preventing future prosthodontic and orthodontic treatment needs make the additional behavior management challenges worthwhile. Thus, behavior

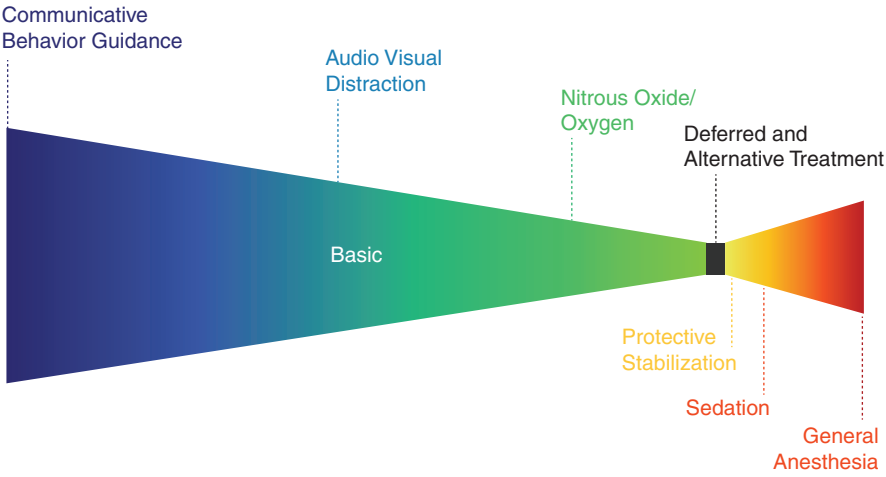


Fig. 5.1 Behavior guidance technique continuum. Source: Nelson (2013). © 2013, Elsevier

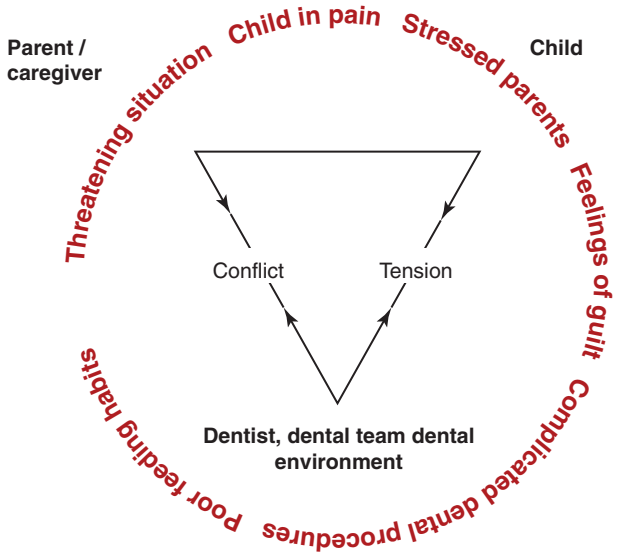
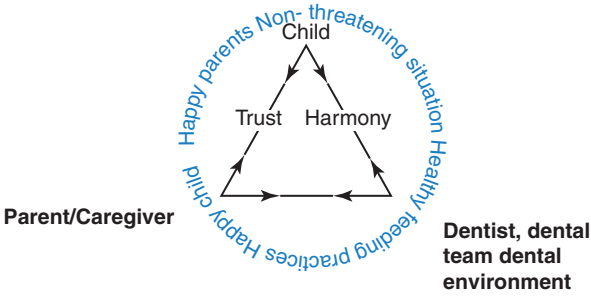


Fig. 5.2 Vicious cycle of poor feeding habits, pain, and parental guilt resulting in conflict between the family and dental team

Fig. 5.3 Alternative environment with healthy feeding practices, lack of pain, and non-threatening environment resulting in harmony between the family and dental team



guidance is central to successful pulp therapy outcomes. Other texts extensively review behavior management, and the focus of this chapter will be on practical techniques to manage children and adolescents undergoing pulp therapy procedures.

Table 5.1 Intake questionnaire. (Source: Kupietzky (2022). © 2022 Wiley Blackwell)

How do you consider your child is learning?	• Advanced in learning • Progressing normally • A slow learner
How has your child reacted to past medical/dental experiences?	• Very well • Moderately well • Moderately poor • Very poor
How would you rate your own anxiety (nervousness, fear) at this moment?	• High • Moderately high • Moderately low
How do you expect your child to react in the dental chair?	• Very well • Moderately well • Moderately poor • Very poor
Has treatment for this problem been previously attempted?	• Yes If yes, please elaborate_____ • No

5.2 Patient Assessment

Prior to treating a patient, the dentist should gather historical information to form a preliminary behavior assessment. Numerous questionnaires exist to assess temperament, fear, and anxiety, but the simple background questions shown in Table 5.1 can yield insight into clinical behavior.

Any answers that suggest potential uncooperative behavior should be discussed with the caregiver where the patient cannot overhear.

5.3 Informed Consent and Parental Guidance

Prior to commencing any pulp therapy procedure, the caregivers of a child must consent to the treatment. Caregivers must understand the value of preserving teeth versus extraction, the goals of the visit, the need for subsequent visits, and the dentist should set a realistic expectation for behavior. All available treatment options as well as expected success rates for the various procedures should be presented and fully discussed. When a child has had a recent trauma or is in pain, it can be difficult for parents to focus on future planning. However, investing the time to establish this therapeutic alliance is critical to prevent misunderstandings in the midst of treatment.

The dentist should identify critical events in the procedure and plan decisions in advance. For example, if behavior is questionable, the dentist and parent may mutually agree that if movement during the injection creates an unsafe environment, the procedure will be aborted, and plans for pharmacologic management will be made. Conversely, a decision may be made in advance that if this type of behavior commences once the pulp is exposed, medical immobilization will be utilized to bring the procedure to a safe completion. Although a caregiver can withdraw consent at

any time, this level of planning helps the parent anticipate potential challenges and commit to a plan of action. All possibilities shall be previously discussed so that lengthy discussions while the child is lying on the dental chair will be avoided.

Providers must also clearly set expectations for caregivers' participation before starting the procedure. Without guidance, caregivers' attempts to comfort their children may inadvertently promote distress. This may include interfering with or contradicting the instructions from the dentist, criticizing the child, or providing uninformative reassurance. The dentist can use data from the assessment questionnaire to probe the caregiver's mindset. If a caregiver identifies they are nervous or do not have confidence in their child's ability to cooperate, then the dentist can inquire if there is someone who can better support the child during the appointment. If there is no one else, the dentist can give the parent the option of being a silent observer while operation is ongoing or waiting outside so the caregiver's own anxieties do not negatively affect the patient. Parents typically respond well to specific instructions on their conduct in the dental environment [3, 4]. Conversely, a parent that demonstrates a natural tendency to engage in coping promoting behaviors (i.e., makes constructive, positive comments, stays silent while the dentist and staff talk) can be used as an asset for distraction and comfort, especially for children with special healthcare needs.

5.4 Basic Behavior Guidance Techniques

5.4.1 Communication

Open, clear communication between the child and dentist is essential to success. The dentist should establish rapport with the child or adolescent before initiating any dental procedures. For young children, the dentist may compliment their clothes or shoes. For older children and adolescents, the dentist may inquire about school or extracurricular activities. These initial conversations should be brief but establish a positive connection and an interest in the patient. The dentist can continue discussing the topic as they move through the typical steps of the appointment (i.e., reclining the chair, examining the teeth, etc.) stopping for explanations when needed. Quiet, calm talk from the dentist can help distract a potentially anxious patient. For timid patients, the caregiver may answer questions on the child's behalf, but it is important to keep all aspects of the conversation patient-centered. The dentist should accompany this communication with frequent, direct eye contact to maintain attention and to monitor for anxiety and pain.

All patients benefit from short, direct instructions, and these are especially beneficial for young children, patients who are non-native speakers, or children with special healthcare needs. Positive instructions are easier for young children to comprehend. For example, "Open your mouth very wide" is preferred to "Don't close." Compliance with instructions should be rewarded with immediate, specific, positive verbal praise ("You are my best patient today because you are keeping your mouth open wide").

"Active ignoring" or "selective attention" should be employed for children engaging in minor, annoying behaviors [5]. By telling a child to stop whimpering, they are inadvertently "rewarding" the behavior by giving it your attention. Instead, the focus should be on rewarding positive behaviors through attention and ignoring negative behaviors, when feasible.

Behavior that interferes with treatment should be addressed by utilizing voice control. Voice control has been mistakenly characterized as yelling at or berating children. Instead, the dentist gains the child's attention through modulating their own voice be it with altered volume, pace, or tone [6]. The child also benefits from an explanation about how complying with instructions will benefit them in immediate and concrete ways. For example, "If you move when I am touching your teeth, I may accidentally touch your gums, which would hurt. When you sit still, I can be gentle." Subsequent compliance with these commands should be immediately praised in a warm, friendly tone.

Patients benefit from a signaling mechanism, typically a raised hand or thumb, in case they need to communicate when they have instruments in their mouth; this has been termed as "stop signals" or "enhancing control" [6, 7]. The dentist should avoid reference to discomfort as a reason to signal (i.e., "Raise your hand if anything hurts"), as the patient will be constantly monitoring for pain increasing hypersensitivity and anxiety. Instead, the dentist can say "Raise your hand if you need to tell me anything." If a patient overuses signals to delay care, the dentist may have to limit how often they will pause, but this technique is usually well received and builds confidence in the dentist-patient relationship.

5.4.2 Tell-Show-Do

In tell-show-do, procedures are described to patients using developmentally appropriate, non-threatening terminology. Relevant instruments are shown to the patient, and the child is able to touch the instrument in a safe manner. Finally, the procedure is performed. For endodontic therapy, rubber dam use has been associated with decreased stress, and with practice, rubber dam placement is fast and leads to optimal visualization, protects the tissues, prevents aspiration, and encourages nasal breathing, which promotes the response to nitrous if being used [8]. Tell-show-do is an ideal technique to promote acceptance of the rubber dam. The rubber dam clamp can be introduced as a "ring" and placed on the child's finger. They should be told that the ring will be snug so it will not fall out and given a small squeeze on the finger or forearm to prepare them for the tight sensation. Next, the rubber dam on the frame is introduced as a "trampoline" for the "sugar bugs" to jump on or as a "raincoat" to keep the teeth dry. For single tooth isolation, it may be easier to place the clamp first (with 18 in./45 cm of floss for easy retrieval) and then to slip the rubber dam around the bow and below the wings. The noise of slipping the rubber dam over the frame can be explained as the sound of fastening buttons on the raincoat.

To reduce alarm from the sharp appearance of instruments such as files, the patient can be shown a paper point. The dentist may let the child hold the paper point and tell them that today you will be using a number of things that look sharp, but they are not "pokey" and that this is an example. Dentists must take safety precautions in case of disruptive behavior and should ligate any small instruments such as broaches and files with floss. Even with rubber dam isolation, there is risk of swallowing or aspiration if a child becomes combative.

5.4.3 Distraction

Of all the behavior guidance techniques, distraction has the strongest evidence of efficacy in improving cooperation and reducing pain perception [9]. Distraction can be verbal, visual, and physical; a combined approach is best. For an initial appointment with a child unfamiliar with dentistry, the dentist must explain new procedures or instruments and may want to use verbal distraction. In addition to tell-show-do, the dentist can use storytelling or a nonverbal guessing game. For example, the dentist may say "I bet I can guess your favorite color. Blink once if my guess is wrong and twice if it is right." These games can engage the child's attention through difficult parts of the procedure. Some children find counting soothing, and when accompanied by a small break, this gives opportunities for escape.

Once a child is more familiar with the dental setting, they may prefer audiovisual distraction utilizing wrap-around eyeglasses or a screen mounted in viewing distance [10, 11]. Use caution with earphones or buds that block the dentist's voice entirely so the patient is not startled by new stimuli. Adolescents tend to prefer bringing their own music to appointments and use of headphones.

Physical distraction can help relieve pain during potentially uncomfortable procedures. Gentle cheek shaking during injection activates nerves that conduct nonnoxious stimuli to close a neural "gate" to prevent nociception [12, 13]. According to "gate theory," vibrating the cheek or the surrounding mucosa tissues may reduce the sensation of pain as postulated by the gate control theory of pain management, which suggests that pain can be reduced by simultaneous activation of nerve fibers through the use of vibration [14]. Vibrating devices have potential to mitigate pain but have mixed results and should not impair the dentist's ability to maintain adequate head control [15]. Children may enjoy having a stuffed animal or squishy toy that they can squeeze to distract them from the discomfort. Finally, engaging in appropriate movements such as circling a foot, raising a leg, or writing in the air using a leg serves as effective distraction for challenging portions of the procedure for limited amounts of time [16].

Some parents are excellent partners in distraction by playing music or engaging in patient-centered discussion with the dental team about the child's interests and accomplishments. As long as the parent allows instructions to come only from the dentist and conversation remains patient focused, this presence can be reassuring.

5.4.4 Relaxation Exercises

For anxious patients, management techniques that promote slow, deep breathing are beneficial [17]. Diaphragmatic breathing, or paced deep breathing, leads to a decrease in sympathetic activation, resulting in physiologic changes such as decreased heart rate [18]. These exercises can be introduced in a number of ways based on the child's developmental level. For younger children, a bubble blower can be introduced prior to the procedure to practice big, deep breaths [19]. Once the appointment starts, they can continue to practice this breathing. A hand can be placed on the abdomen to encourage "belly breathing" or deep breathing. The dentist can take breaths together and count slowly to lower the rate of breathing.

5.4.5 Nitrous Oxide

If available, nitrous oxide is a valuable adjunct to pulpal therapy although it is no replacement for behavior management and profound local anesthesia. Nitrous oxide reduces anxiety, raises the pain reaction threshold, obtunds the gag reflex, and can encourage deep breathing and support distraction techniques [20–22].

5.5 Pain Validation

Some patients have a difficult time differentiating stimuli such as pressure or handpiece vibration from pain. Prior to any operative procedure, the dentist should run the handpiece in the mouth without touching the tooth to gauge the child's reaction. Teeth with irreversible pulpitis have been characterized as "hot teeth" and can be painful even with excellent anesthesia technique [23]. The dentist can apply refrigerant (Hygienic® Endo Ice®, Coltene/Whaledent Inc., Cuyahoga Falls, Ohio, USA) to a tooth following local anesthesia and prior to any procedures. If the tooth responds to cold, additional measures are indicated. If there is no sensation, the dentist can proceed with gently using a slow-speed bur on intact enamel [24]. If there is a negative reaction, it is likely the result of procedural anxiety versus true perception of pain. For more information on local anesthesia, see Chap. 4.

5.6 Management of Challenging Situations

5.6.1 Inability or Refusal to Cooperate

Some children or adolescents are unable or unwilling to cooperate for dental treatment. This behavior, especially in the circumstances of recent trauma or pain, has a foundation at least partially in dental fear. However, inappropriate child/adult relationships, desire for attention, and attempts to assert dominance/defiance can result

in a child that is mistrustful or unwilling to engage in fear reduction exercises and thus cannot cope with treatment. Management of these patients is dependent on patient factors such as age, cognitive development, and type/intensity of response as well as tooth-related factors such as complexity of needed ideal treatment and risks of alternative treatment.

The first step in managing any uncooperative behavior is to establish communication. For patients with exaggerated externalizing behaviors, sometimes dubbed as "temper tantrums," a time-out may curtail this behavior and open communication [25]. For shy or timid children, gentle communication and gradual exposure to the environment can build trust. For these children, humor, such as asking them to take off their shoes so you can count their teeth, can result in wide open mouths eager to prove where teeth are found [26, 27].

If behavior management strategies are inadequate to establish a safe environment for complex procedures, the provider should consider deferring treatment until it can be safely performed under sedation or general anesthesia. In patients with severely carious first permanent molars, which would require multiple endodontic therapy and restorative visits per tooth, alternatives such as extraction with second molar substitution could be considered [28].

5.6.2 Inadequate Pain Control

In some circumstances, local anesthesia is either exquisitely painful or cannot be reliably obtained at all due to infection. For single-rooted necrotic teeth with extensive local swelling, pulpal access may be more comfortable without local anesthesia. Sensibility testing should occur prior to access to confirm lack of innervation, and conservative instrumentation should be utilized. Upon access to the pulp chamber, these patients may communicate a sense of released pressure or immediate pain relief. Definitive cleaning and shaping can occur at a later date when adequate periapical anesthesia is possible. This technique may be used in molars but is not as predictable as vital pulp tissue may still reside in one canal.

In circumstances of "hot teeth" where pain control is inadequate, the dentist may manage with analgesics and antibiotics, if indicated, until the infection is no longer interfering with treatment or until sedation or general anesthesia is possible.

5.7 Recovery After a Difficult Appointment

Dentists often treat children and adolescents who have had previous negative appointments. These may have occurred with a previous dentist or in their own office when an emergency necessitated treatment in an un-ideal situation or a patient lost cooperation during a visit. Locker et al. [29] found slightly over half of patients with dental anxiety had onset in childhood and aversive events in childhood were most strongly associated with anxiety.

Previous negative experiences do not have to define a child's future relationship with dental care. Appropriate management can prevent or reframe unpleasant memories with the goal of instilling a positive dental attitude.

Negative appointments should be discussed with parents as soon as feasible. If the unpleasant visit happened elsewhere, discussion of appointment details should be part of the intake interview where the child cannot overhear. If it happens in your office, the dentist should engage with the caregiver immediately after the appointment. If it is possible to separate the child from the parent, it is preferable this conversation take place in person, and if they cannot be separated, a phone call should be scheduled the same day as the appointment. At this time, the dentist should ask open-ended questions about the appointment to assess any parental concerns. These are best addressed immediately to assuage any apprehensions about the visit before they have time to turn to dissatisfaction. The dentist can communicate that the appointment was difficult, but necessary, empathize that parenting is demanding, and compliment the parent on specific ways they helped the child cope. Next, the dentist and parent should discuss communication strategies. Caregivers should never bring up difficult aspects of the appointment in the future. A toddler may not remember they required active immobilization during an injection, but if they are told the story about being "held down" repeatedly, this "memory" will become vivid. For school-age children and adolescents who vocalize fear, communication should focus on successful aspects of the visit and how much the team cares about the patient.

Pickrell et al. [30] described a formal process of memory restructuring that can help reframe unpleasant visits. This technique can be taught to parents new to your office or introduced following an avoidable, difficult appointment. First, a visual reminder of a time the child was happy at the dentist is used. This could be the initial patient photo or even a picture of the child brushing their teeth. Second, the child is asked to verbalize something positive about their previous visit and to practice sharing this information with a caregiver. The dental team then reinforces this positive feedback with specific examples of cooperation such as the child's ability to hold hands in their lap. Finally, the child demonstrates these behaviors, demonstrating they can achieve a successful dental visit. Pickrell [30] found that children who underwent this process were significantly less likely to report pain for fear of an injection.

5.8 Conclusions

Management of endodontic treatment in children and adolescents is inherently challenging due to the complexity of procedures and increased likelihood of pain. With proper communication, use of behavior management techniques, and appropriate post-visit guidance, endodontic therapy can be successfully performed on a wide spectrum of patients. If a dental home is established prior to the endodontic treatment, the environment facilitates optimal behavior. Unfortunately, children who appear with acute pain usually do not have a dental home and are unlikely to return

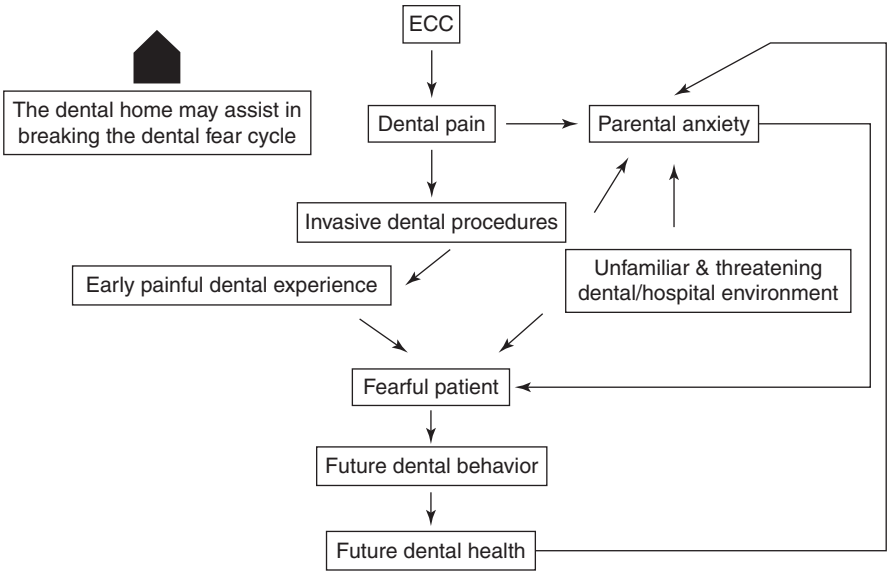


Fig. 5.4 A dental home is key to breaking the cycle of dental pain and dental fear

for routine exams without guidance. If a dental home has not been established prior to treatment, a child's best way to overcome a prior negative dental experience is to develop a healthy pediatric dental treatment triangle with a kind dentist and warm dental team (Fig. 5.4).

5.8.1 Case 5.3

Two 4-year-olds arrived at the pediatric dentist's office following a collision of heads at nursery school. Both children had bleeding from the mouth and were accompanied by their parents. Sue had been at the dentist initially at age two and had since returned for a checkup the previous year. Jack had never been to any dentist, and this emergency visit was the first for both himself and his mother. Jack was crying and very frightened, and his mom was visibly upset and tense. Conversely, Sue was a little nervous but was familiar with the office, staff, and dentist. She was looking forward to receiving the prize to be given later. Her mom remembered being told by the dentist that such incidents might occur and are indeed expected. "Kids will be kids. Maybe that is why they grow up with baby teeth." On the other hand, Jack's mom reacted aggressively toward the dentist when she was told that her son's lip was indeed lacerated but that his teeth were not fractured due to the fall; rather they were severely decayed and only appeared broken. The mother had given Jack a baby bottle of apple juice to calm him. She was shocked when told that Jack needed extensive dental work not only on his front teeth but also his molars, as they showed advance signs of ECC.

Sue was discharged after an X-ray. Jack refused to take an X-ray and was to return for restorative treatment under general anesthesia, his parent's preference.

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6 The Caries Lesion: Diagnosis, Decision-Making, and Recommendations for Lesion Management

Fernando Borba de Araujo, Marisa Maltz, Cleber Paradzinski Cavalheiro, and Tathiane Larissa Lenzi

Contents

6.1 Introduction

Dental caries is a biofilm-mediated, diet modulated, multifactorial, noncommunicable, dynamic disease, resulting in net mineral loss of dental hard tissues [1]. It is affected by biological, behavioral, psychosocial, and environmental factors. Caries lesions develop as a consequence of this process.

Caries diagnosis is the clinical judgment integrating available information, including the detection and assessment of caries signs (lesions), to determine presence of the disease. The main purposes of clinical caries diagnosis are to achieve the best health outcome for the patient by selecting the best management option for

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each lesion type, to inform the patient, and to monitor the clinical course of the disease [2, 3]. Minimally invasive interventions have been proposed for caries management, comprising early detection, preventive procedures, and minimally invasive treatment procedures [4]. This chapter will discuss aspects related to caries diagnosis, decision-making, and recommendations for management of initial, moderate, and extensive caries lesions reaching the outer half of dentin. Deeper dentin caries lesions will be addressed in Chap. 10.

6.2 Caries Disease Development and Control Strategies

Biofilms are complex microbial communities embedded in a matrix of self-produced polymer substances. Biofilm formation constantly occurs both on smooth surfaces and on more retentive and anatomically complex areas, and cannot be avoided. The metabolic activities of the active bacterial deposits, favored by the frequent consumption of fermentable carbohydrates, especially sucrose, affect the underlying tooth surface, resulting, over time, in irregular pH fluctuations that can result in mineral loss and establishment of the disease. There is evidence that the first clinical signs of enamel demineralization are observed after drying of the surface after only two weeks from the beginning of biofilm construction [5]. However, after a single week of uninterrupted biofilm formation, it is already possible to detect increased enamel porosity, which becomes more obvious over time [5, 6]. After three or four weeks, opaque areas can be observed even without drying of the surface, being located in the regions covered by the biofilm and following the direction of the enamel prisms [7]. The detection of initial caries lesions represents a major challenge for clinicians, because such lesions may go undetected or may be mistaken for defects in enamel development, such as fluorosis or hypomineralization. However, the rate of progression of these is relatively low, especially in children who do not present dentin cavitation [8]. Currently, according to the best available evidence, the detection of initial caries lesions must be part of the clinical routine, so that therapeutic measures can be taken to further reduce the risk of progression of these lesions. If the disease is not controlled, the formation of dentin cavitation is the natural consequence that leads, in the absence of treatment, to tooth loss. Although biofilm is constantly formed and the demineralization and remineralization process cannot be prevented, the effect of the biofilm on the dental surface can be decreased by control measurements, and metabolic processes can be modified. The development and progression of caries lesions can be prevented or controlled, regardless of the presence of cavitation and patient age. Caries management consists of actions taken to interfere with mineral loss at all stages of the caries disease [9], including both operative and non-operative interventions. Because of the continuous de/remineralization processes, caries control needs to be sustained throughout life. Strategies for caries management include population and/or individual targeted approaches. According to the World Health Organization, population-based strategies should prioritize common risk factors with other noncommunicable diseases associated with excessive sugar consumption, such as cardiovascular disease,

diabetes, and obesity [10]. In this context, practices related to lifestyle, such as healthy diet and improvements in social determinants, such as educational level, housing conditions, and access to health services, all impact these diseases.

Individual-based strategies are focused on the specific individual's caries risk. These approaches, however, should be implemented only after proper clinical examination and classification of the caries lesions based on severity and activity status.

The presence of active caries lesions reflects the mineral imbalance, favoring the mineral loss over gain. Therefore, measures for controlling etiological factors (diet and biofilm) and those that interfere with the disease process, such as fluorides supply, aim to re-establish the balance between episodes of mineral loss and gain and are essential to arrest caries lesion progression. The disease may be controlled exclusively through the treatment of caries lesions or necessitate specific complementary interventions, described throughout this chapter.

6.3 Caries Diagnosis

Caries diagnosis process must take into account not only caries lesion detection but also the etiologic factors of dental caries and caries activity as manifested by the lesions.

The best method for caries lesion detection and assessment is visual inspection aided by a ball-ended probe [11] and must be performed for all patients. The use of indices, such as the international caries detection and assessment system (ICDAS), improves the diagnosis process mainly in terms of sensitivity and reliability [12]. The presence, severity, and activity of lesions must be assessed through visual inspection. The most widely used adjunct method for detecting caries lesions is the radiographic examination. Its implementation as an adjunct to visual inspection facilitates the monitoring of lesion progression [13, 14] and improves the estimate of the depth of the lesion rather than relying on visual inspection. However, the method tends to underestimate the actual mineral loss from the lesion and is not suitable for detecting the early stages of lesion development [13].

Caries lesion activity assessment seeks to differentiate caries lesions deemed active from those deemed inactive in order to provide optimal care planning aimed to arrest active lesions. Activity status of a caries lesion is defined by surface characteristics [15]. Clinical surface features, such as change of texture, translucency, and color, and other factors such as presence of thick plaque and plaque stagnation areas as well as gingivitis all help assess whether a lesion is progressing or non-progressing/arrested [16–18].

On clinical examination, the first signs of tooth demineralization are visualized as whitish opaque areas, which become even whiter and more evident as the surface dries. These lesions, when there is still no loss of surface continuity, are classified as active non-cavitated lesions (ICDAS scores 1 and 2). If the process is not controlled and the lesions progress, the surface layer ruptures, and cavitated enamel lesions (ICDAS score 3) are created, preserving the same clinical characteristics

that indicate the presence of activity (Fig. 6.1a) (white, opaque, and rough enamel). If the disease process is controlled, enamel lesions may assume clinical characteristics of inactive lesions (Fig. 6.1b), with recovery of gloss and surface smoothness. They can maintain their whitish appearance, take on a darker or brownish coloration, or even disappear due to polishing/superficial wear. Lesions closer to the cervical margin tend to be active, whereas enamel lesions that are distant from the margin tend to be inactive. Teeth in infra-occlusion are more likely to have active lesions because of the greater propensity for biofilm accumulation. Underlying dark shadow lesions from dentin (Fig. 6.2) are classified as ICDAS score 4 and present clinically as discolorations from the dentin in different shades of gray, blue, or brown, visible through the translucency of the enamel, with or without localized enamel breakdown [19]. Despite their clinical appearance, which in many situations leads the clinician to consider a large involvement of the coronal dentin, studies

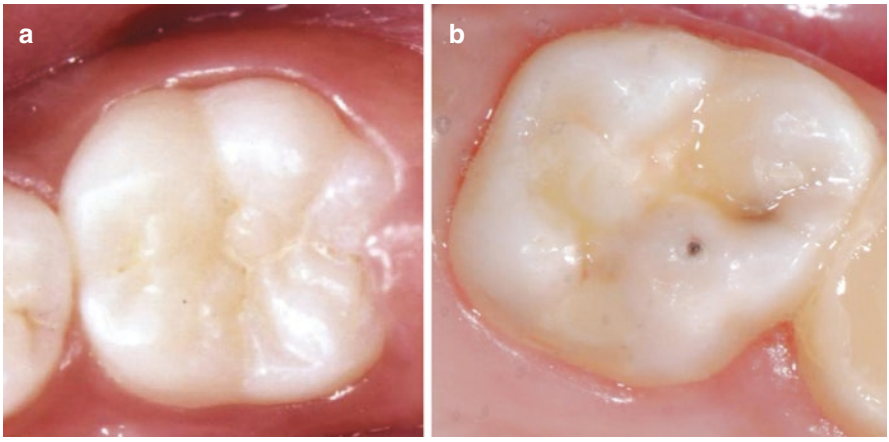

Fig. 6.1 Active initial caries lesion on the occlusal surface (**a**). Inactive caries lesion (**b**)

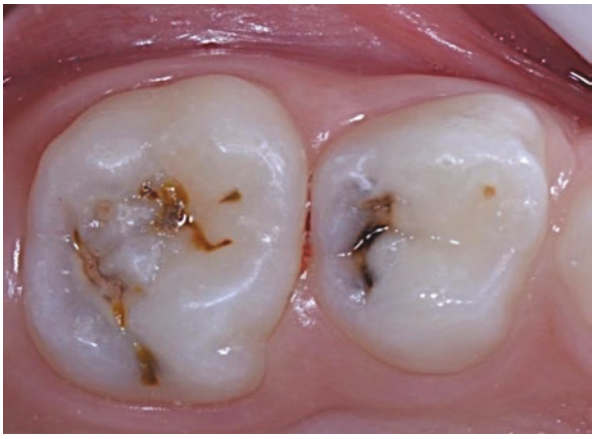

Fig. 6.2 Underlying dark shadow lesions from dentin in primary molars

have shown that most underlying dark shadow lesions (67.4–78.9%) in permanent teeth do not present radiographically detectable radiolucency in dentin [20, 21]. However, these are lesions with a complicated prognosis, since about half of them progress to more severe stages [8, 22]. Thus, this is one of the situations in which a complementary radiographic examination is beneficial for determining the depth of the lesion and, consequently, the best treatment. Dentin caries lesions may be classified as ICDAS score 5 for distinct cavity with visible dentin or ICDAS score 6 for extensive distinct cavity with visible dentin (involving more than half of the surface) [19]. Active dentin caries lesions (Fig. 6.3a) present softened tissue, usually yellowish or brownish with a moist appearance and opacity in the adjacent enamel. The inactive ones (Fig. 6.3b), on the other hand, have hardened tissue and are usually darker, with a dry aspect. The hardness criterion prevails over that of coloration and moisture [23]. The American Academy of Pediatric Dentistry (AAPD) suggests that radiographs be taken in all situations where tooth surfaces cannot be visualized, regardless of signs and symptoms [24]. However, the current clinical guidelines of the European Academy of Paediatric Dentistry (EAPD) [25] and the Brazilian Association of Pediatric Dentistry [26] note significant changes regarding the radiographic evaluation as a complementary method to detect caries lesions. EAPD [25] suggests that methods free of ionizing radiation, such as tooth separation and fiber-optic transillumination, be used in cases of interproximal lesions detected on clinical examination (cavitated or non-cavitated). It is also suggested that radiographic examination be indicated in the presence of active caries lesions, both non-cavitated and cavitated. Furthermore, the authors emphasize that caries risk/activity should be regularly evaluated as it may influence the indication for initial and monitoring radiographic examinations. While the EAPD and AAPD recommend radiographs to monitor caries activity and risk at key ages of the patient (5 years, 8–9 years, 12–13 years, and 15–16 years of age) [24, 25, 27], the guidelines of the Brazilian Association of Pediatric Dentistry [26] are even more conservative. They focus on minimizing the use of methods involving ionizing radiation and are aligned with the minimally invasive dentistry philosophy. They consider radiography only as a

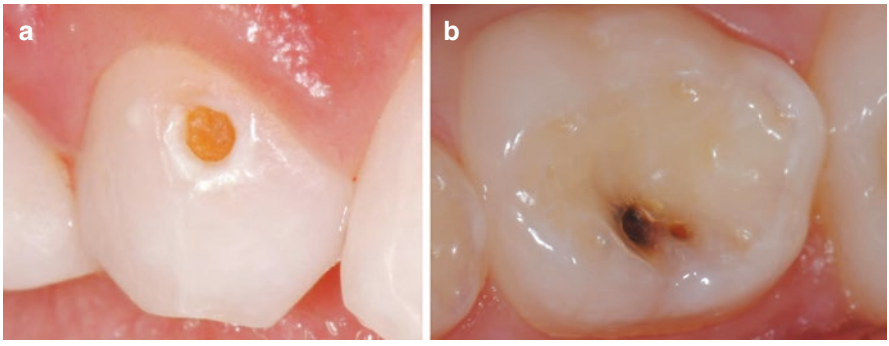

Fig. 6.3 Cavitated denti lesion in the vestibular surface is active (**a**). Inactive caries lesion on occlusal surface (**b**)

confirmatory method recommended for cases in which cavitated or underlying dark shadow lesions from dentin lesions are detected in the clinical evaluation, and the clinician is in doubt about the treatment [26, 28–30].

Although proximal lesions can also be assessed by visual evaluation with the aid of ICDAS, these lesions only become visible by the time they are large enough to show through the enamel or marginal ridge. A solution to the difficulty in visual detection of proximal lesions is the use of interproximal radiographic examination that identifies more lesions than the visual evaluation [31]. The indication for radiographic evaluation of interproximal caries lesions in pediatric dentistry is the presence of several clinical signs. These signs are the presence of caries lesions and/or restorations in free smooth surfaces, patient caries activity, and high rates of biofilm and gingival bleeding, especially in proximal sites. Only 10% of lesions in primary teeth radiographically located in enamel are cavitated, while 50% of lesions located in the outer half of dentin already present clinical cavitation [32]. Thus, in the scenario of radiographically detected caries lesions not reaching inner half of the dentin, temporary separation with elastic bands has been suggested for direct visualization of the proximal surface, enabling the evaluation of the presence or absence of cavitation and consequently the disease activity. Therefore, visual inspection should be the main method for detection of caries lesions, while complementary methods such as radiographic examination should be used to assist in treatment planning. New technologies for caries detection have been developed and studied. Fluorescence-based methods to aid the detection of caries lesions are based on the principle that decayed dental tissues have their fluorescence properties altered in comparison to healthy dental tissues [33–36]. However, no significant benefit has been shown that justifies their use in daily clinical practice [11].

6.4 Strategies of Dental Caries Lesion Management

Before addressing in detail the concepts and guidelines related to the management of caries lesions, it is necessary to categorize the different strategies for this purpose. For this, we followed the principles of minimally invasive dentistry that classify the disease control strategies and clinical management of caries lesions into categories according to the degree of hard tissue invasion [37, 38]:

Noninvasive interventions: These do not involve the removal of hard tooth tissue, only dietary and hygiene guidance and professional fluoride application.

Micro-invasive interventions: When mineral removal of tooth structure is involved, usually during acid etching. Sealants and resin infiltrants are used.

Invasive interventions: Mechanical removal of tooth tissue by hand instruments and/or diamond rotary/drill burns.

Two strategies, non-restorative cavity control (NRCC) [39] and Hall technique [40], do not fit into any of the above categories and are defined as “mixed interventions” [38]. The caries lesion depth is a criterion in clinical decision-making, although it should never be considered by itself, but adjacent to other criteria. Identifying whether the lesion is restricted to enamel or involving dentin is a way to

infer its prognosis, since enamel lesions tend to progress slowly due to the composition of the tissue [41]. Furthermore, the presence of cavitation may influence lesion progression since it causes biofilm retention. Thus, when faced with a caries lesion, the clinician should ask himself, in view of the restorative decision: "Is it a cavitated lesion?" If the lesion is cavitated, the next question is: "Is the lesion active?" With active lesions, the first concern is to control the activity, and this leads to a new question: "Can the lesion be inactivated without restoration?" To answer this question, biofilm control settings of the lesion should be evaluated. If a cavitated lesion allows direct access for brushing, one may choose to postpone the restorative procedure until the etiological factors are successfully controlled or even choose not to perform it (i.e., nonrestorative cavity control). For this to be possible, the patient and the caretakers need to be motivated to control the caries activity, and this motivation includes understanding the health process versus caries disease. Once the caries activity is controlled, the loss of dental structure must be evaluated, considering the need to establish form, function, and esthetics. Some questions must be pondered: "Does the destruction due to caries compromise occlusion, chewing, phonation, or the patient's social life?" "Does the family or the patient himself demand esthetic improvement?" "Is there proximity to the dentin-pulp complex causing sensitivity?" Another aspect to be taken into consideration, in the case of primary teeth, is how long these teeth will remain in the oral cavity and their strategic importance [42]. In the context of treatment choice, it is important if the first permanent molar has already erupted, or not. Caries lesions on proximal surfaces deserve attention because they cannot be directly visualized. In these cases, it is important that the clinician understands the correlation between the radiographic image and the clinical aspect for appropriate decision-making, as discussed previously in this chapter. On proximal surfaces, the presence of a cavity is a crucial factor for the indication of micro-invasive or invasive strategies, depending on the lesion depth and difficulty (or even impossibility) of biofilm control by the patient on these surfaces. It is important to emphasize that restorative procedures, by themselves, do not treat the disease [43] but aim to control the lesion progression when the removal of biofilm by the patient is not possible, making it necessary to protect the dentin-pulp complex and restore the integrity of teeth affected by caries [44]. Noninvasive strategies and monitoring of caries lesions necessarily involve knowledge of the progression pattern in primary and young permanent teeth, highlighting the importance of variables such as the presence or absence of cavity, lesion depth, patient's past and current experience of caries activity, access to fluoride, and the patient's hygiene pattern.

6.5 Treatment Options for Initial, Moderate, and Extensive Caries Lesions

The International Caries Classification and Management System (ICCMS), integrates ICDAS scores with more extensive patient-level information for caries management. Non-cavitated enamel caries lesions are classified as initial stage decay,

localized enamel breakdown and underlying dentin shadow lesions are categorized as moderate stage decay, and cavitated dentinal caries lesions are categorized as extensive stage decay. Although ICCMS was not yet validated for treatment purposes, it recommends that active initial lesions be managed with noninvasive or micro-invasive treatments, while active moderate lesions should be managed by micro-invasive or invasive treatments [45]. Restorative procedures are indicated for extensive caries lesions, and if restorative care is not possible, clinicians should consider the Hall Technique or extraction [45]. Nevertheless, it is important to emphasize that the mere presence of mineral loss in dentin does not indicate the need for operative treatment. The treatment decision should be individualized and based on the assessment of the patient's caries activity and caries risk (e.g., sucrose and fluoride exposure, oral hygiene habits and previous history of the disease). Due to the multifactorial nature of the caries disease, it is important to know which factors are imbalanced and consequently lead to the development and progression of caries lesions in each specific case. In addition, one should take into account other factors that may influence the treatment decision, such as esthetics, chewing function, and pain sensitivity. Treatment of dental caries needs to be more comprehensive than simply focusing on teeth surfaces (Figs. 6.4 and 6.5). So we elaborate here on the logical reasoning to guide the clinical decision-making.

No treatment is necessary for sound tooth surface (ICDAS score 0). Monitoring is needed to evaluate whether the surfaces remain caries-free over time. It is important to emphasize, however, that patients with sound or no caries activity should receive basic prophylaxis and information about the etiological factors of the disease and be coached on the importance of adequate oral hygiene, healthy diet, and regular use of fluoride (fluoride toothpaste).

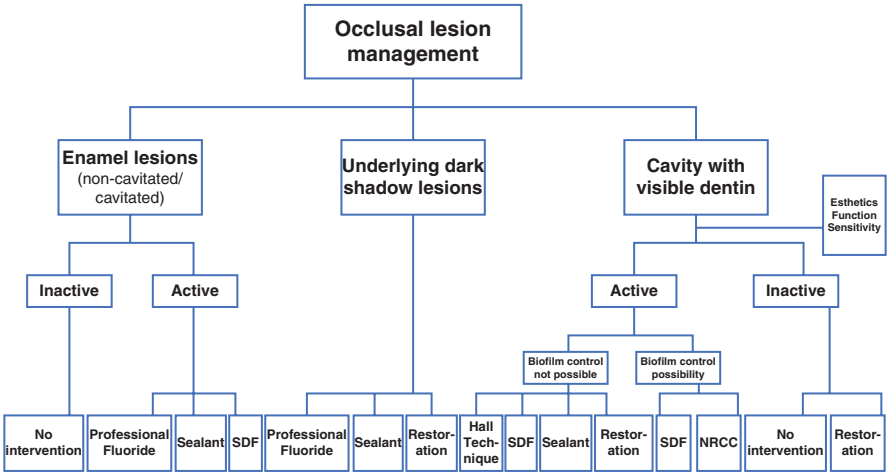

Fig. 6.4 Treatment possibilities for the management of occlusal caries lesions (disease control is essential for intervention success. Every patient, regardless of the clinical status of the lesion, should be monitored)

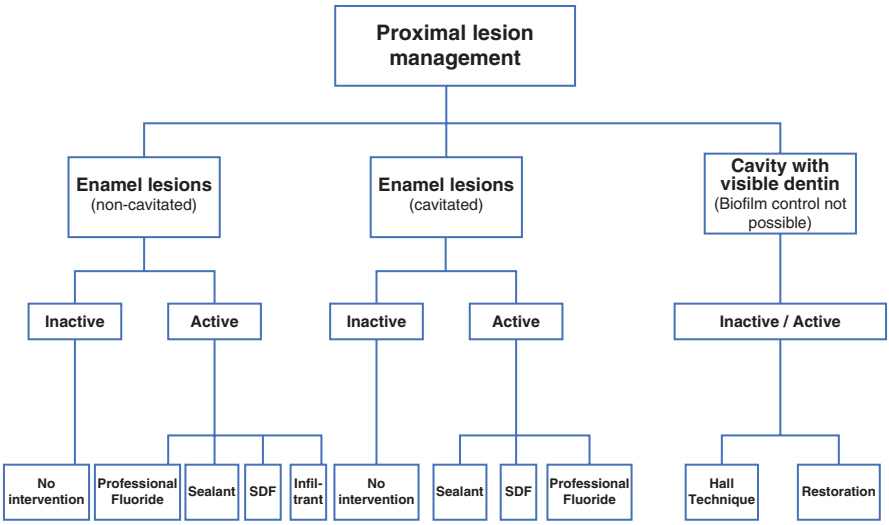

Fig. 6.5 Treatment possibilities for the management of proximal caries lesions (disease control is essential for intervention success. Every patient, regardless of the clinical status of the lesion, should be monitored)

Active initial lesions, such as a first visually noticed change in enamel (ICDAS score 1) and a distinct change in enamel when viewed wet (ICDAS score 2), can be treated by focusing exclusively on disease control with noninvasive methods at the patient level. However, considering the patient profile and the tooth surface, adjuvant micro-invasive methods can be used. Regular use of fluoride toothpaste of at least 1000 ppmF [46] and professional topical fluoride applications complemented with professional biofilm control are noninvasive approaches [47]. When the child is not able to self-care, the use of fluoride toothpaste twice a day in small amount is the responsibility of parents or caregivers.

Professional prophylaxis followed by topical professional fluoride applications (acidic gel, FFA 1.23%) in an average of four applications is indicated when caries activity is prevalent in all quadrants. Varnishes are indicated when caries lesions are located in specific teeth, complemented with professional biofilm control, mediated by the visible plaque index and gingival bleeding index [47]. The use of silver diamine fluoride (SDF) may also be an option for arresting enamel caries lesions in primary teeth since it has been shown that the semiannual application of 38% SDF and 5% sodium fluoride varnish had similar effectiveness [48]. A targeted approach to dietary control should also be considered and aim to reduce sugar intakes via food or drinks [49]. Sealants can be used for controlling initial lesions on occlusal [50] and proximal [37] surfaces. Resin infiltrant is an alternative treatment recommended only for treating non-cavitated lesions on proximal surfaces extending into the inner half of enamel up to the outer half of the dentin [51]. The limited number of studies evaluating outcomes, such as open cavitation, makes it unfeasible to

recommend a specific management approach for initial caries lesion control in primary teeth [52].

Inactive non-cavitated enamel lesions, regardless of the surface where they are located (occlusal or proximal), do not require any type of intervention, except for esthetic reasons in anterior teeth.

Moderate lesions, such localized enamel breakdown in opaque or discolored enamel (ICDAS score 3) may be treated by the noninvasive approaches mentioned above. Most of the time, cavitated lesions provide an additional niche for biofilm retention, and it may not be possible to remove it effectively with the bristles of the brush. In these situations, blocking with resin sealant (Fig. 6.6) is recommended. The treatment decision for underlying dark shadow from dentin with or without localized enamel breakdown (ICDAS score 4) depends on the lesion's depth. For this, interproximal radiographic evaluation is recommended. Micro-invasive (resin sealant or flowable resin composite) or noninvasive approaches can be recommended for lesions without radiolucency at the dentin, with radiolucent image at the enamel-dentin junction or at the outer half of the dentin. Despite the lack of evidence on the sealing of underlying dark shadow from dentin lesions in permanent teeth, previous studies have demonstrated the effectiveness of this technique for controlling cavitated dentin caries lesions with moderate radiographic depth (up to the outer half of dentin) [53–55], and similar results have been described for primary teeth [56]. Invasive treatment (selective carious tissue removal and adhesive restoration) can also be indicated for treating ICDAS 4 lesions exhibiting radiolucency at the outer half of the dentin. Restorative treatment is indicated for such

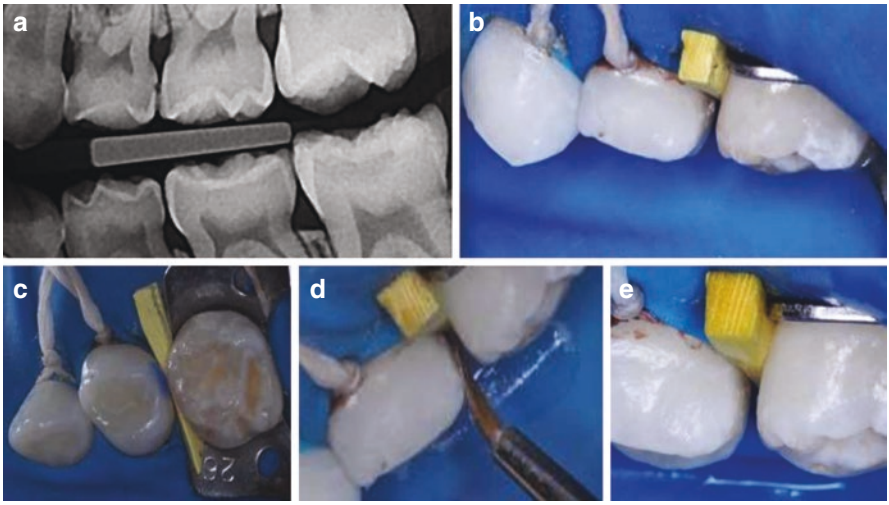

Fig. 6.6 Proximal resin sealant, radiographic appearance (**a**), Microcavitated active enamel lesion on proximal surface with pre-wedging for direct access (**b**), Acid etching with phosphoric acid (Ultra-Etch™, Ultradent), adhesive system application (Scotchbond Universal, 3M Oral Care), and immediate "drying" with microbrush, followed by light curing (**c**), Application of flowable resin composite (Filtek Z350 XT, 3M Oral Care) as a proximal sealant (**d**), Immediate appearance (**e**)

lesions radiographically shown to reach the inner half of the dentin, due to the possibility of lesion progression or surface fracture resulting from lack of enamel support. Minimal intervention procedures in deep dentin will be discussed extensively in Chap. 10. It is important to emphasize that clinical evaluation of the activity of underlying dark shadow from dentin lesions is not possible due to visual and tactile inaccessibility to dentin tissue (although clinical characteristics of the overlying enamel may provide useful information). Since there are no longitudinal studies to date evaluating the pattern of progression of underlying dark shadow from dentin lesions, if there is radiographic evidence of the lesion, the assumption is that such lesions may be progressing and therefore have to be arrested (by sealing or restoration, depending on the radiographic depth). For severe lesions, such as distinct cavity with visible dentin (ICDAS score 5) and extensive distinct cavity with visible dentin (ICDAS score 6), the treatment decision also depends on the lesion's depth. One of the recommended protocols for cavities (ICDAS score 5) on occlusal surfaces restricted to the outer half of the dentin with a diameter of up to approximately 3 mm (extent) on primary and permanent teeth without painful symptoms or pulpal involvement is resin sealant (Fig. 6.7) [38, 56, 57]. It is also suggested to seal cavities of up to 5 mm [57], since we have the possibility of using materials with better mechanical properties such as flowable resin composite [58]. It should be noted that the extent of the lesion is one of the determinant factors of treatment failure [59]. Finally, when opting for more conservative treatments, regular follow-ups are essential to control for possible clinical failure of the sealant [54, 55] and the need to repair the material [23]. If the decision is to perform restorative treatment, whether by the conventional restorative approach or by atraumatic restorative treatment (ART) that uses only manual instruments to access and clean the cavity [60, 61], selective carious tissue removal must be chosen [62]. Additionally, it is of paramount importance that the clinician performs a careful assessment of the pulpal condition. This issue will be discussed in Chap. 10. Until recently, the possibility of not restoring a cavitated dentin lesion was considered unacceptable. However, with the knowledge acquired in the last decades regarding the evolution of the disease, along with the evidence provided by clinical studies, the "sealing" of the caries lesion presenting open cavitation with a steel crown without previous removal of the caries tissue (Hall technique) is a possibility with proven effectiveness [40], being a technique of easy execution and low cost that preserves the dental structure [63]. Hall technique has demonstrated lower chance of failure when compared with non-selective removal and conventional restorations for treating cavitated but not deep lesions in primary teeth [64]. Non-restorative cavity control (NRCC) has been recommended for primary teeth [65] and for specific cases in permanent teeth [39], aiming to control lesion progression. In clinical practice, this approach is a more conservative treatment option, whereby invasive procedures can be postponed or even avoided. It can also be indicated for more specific clinical situations, such as difficulty in patient cooperation with conventional restorative treatment, very large and expulsive cavities in primary teeth in which a conventional restorative treatment is highly likely to fail, short time to primary tooth exfoliation, and locations where conventional treatment is difficult to access. However, it is of great importance to

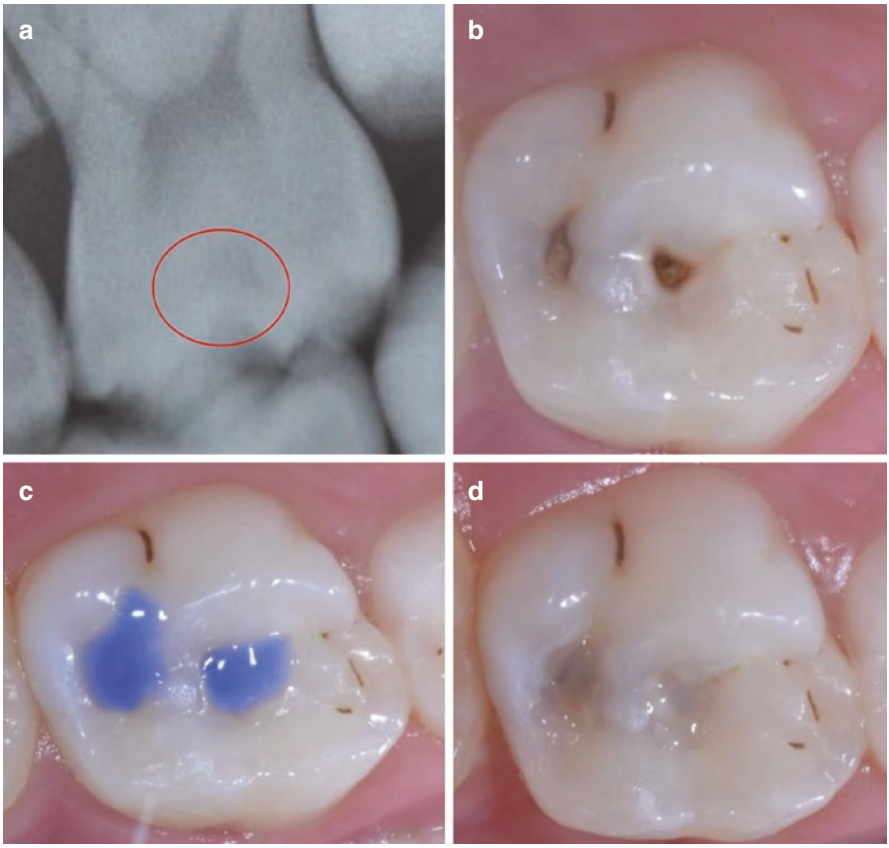

Fig. 6.7 Occlusal resin sealant for treating active cavitated dentin lesion (**a**), Radiographic appearance at outer half of the dentin (**b**), Acid etching with phosphoric acid (Ultra-Etch™, Ultradent), followed by adhesive system application (Scotchbond Universal, 3M Oral Care) (**c**), Tooth appearance after application of flowable resin composite (Filtek Z350 XT, 3M Oral Care) as sealant (**d**)

establish adequate communication with parents and/or caregivers, since biofilm removal is the basis for the success of this type of therapy [39]. Based on very low certainty of evidence, there is no significant difference in the chance of failure between NRCC and nonselective removal and conventional restoration for non-deep lesions in primary teeth. Otherwise, a lower number of failures have been observed with Hall technique than NRCC in primary teeth [64]. From an orthodontic standpoint, the treatment protocol that consists of cleaning medium- and large-sized occlusal and proximal cavities in primary teeth that are left open with toothbrush and fluoride toothpaste and restoring small-sized cavities with the ART method does not differ significantly from the traditional amalgam and ART restorative protocols with respect to intra-arch distances and malocclusion [66]. The use

of SDF to control cavitated dentin lesions has also been proposed, especially for primary teeth [67]. It is a cariostatic agent, which promotes the remineralization of the dental structure, protecting the collagen fibers, besides having an antibacterial effect. Scientific evidence suggests that SDF arrests dentinal caries lesions in primary teeth better than treatments such as fluoride varnish and ART restorations [68]. It can be found in different concentrations, but 38% SDF has been shown to be more effective than 12% SDF for arresting active cavitated caries lesions in primary teeth [69]. The application of the SDF solution is easy, less costly [70], and painless. There is no need to remove carious dental tissues before the SDF application, which simplifies the treatment procedure and reduces patient discomfort. Thus, SDF can be a promising strategy to control dental caries, mainly in very young and difficult-to-manage children (see Chap. 8).

6.6 Concluding Remarks

- The understanding that dental caries and caries lesions are not synonymous is of fundamental importance for the control of the disease and management of its sequelae. The treatment process starts with an accurate diagnosis that takes into account the caries activity of the individual.
- The clinical approach to caries disease and its consequences should be based on the principles of the minimally invasive dentistry, always adopting noninvasive treatment measures for caries lesions (brushing with fluoride toothpaste of at least 1100 ppm, reducing the consumption of sugars, and supplementing with professional fluoride).
- For treatment of non-cavitated active occlusal caries lesions (ICDAS score 1 and score 2), cavitated enamel lesions (ICDAS score 3), or underlying dark shadow from dentin (ICDAS score 4) reaching the outer half of the dentin, micro-invasive approach (sealing) is recommended.
- For proximal non-cavitated caries lesions (ICDAS score 1 and score 2), noninvasive or micro-invasive treatment is suggested.
- When there is doubt about the presence of cavitation on the proximal surface in the radiographic image with radiolucency at dentin (ICDAS score 4), the clinician should validate it by temporarily separating the teeth for up to 48 h. In the presence of cavitation, if the clinician decides to use micro-invasive approach, it is imperative to avoid retentive interfaces for oral biofilm accumulation, to reduce the risk of adjacent caries lesions.
- In lesions with distinct cavity with visible dentin (ICDAS score 5), cavities on occlusal surfaces located on the outer half of the dentin with a diameter of up to approximately 3 mm (extent), a micro-invasive approach can also be used.
- When invasive intervention is necessary for dentin lesions, selective removal of caries tissue should be the method of choice, since nonselective carious tissue removal is contraindicated (overtreatment).

- The decision for minimally invasive restorative techniques has the advantages of low cost, shorter clinical time, and greater patient compliance. These restorative techniques are strongly recommended as they preserve healthy dental tissue throughout the patient's life.

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Pulp Response to Clinical Procedures and Dental Materials

7

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7.1 Introduction

For decades, bacteria and their products were considered as the main responsible for pulpal breakdown. In that time, it was stated that rather than dental materials and their components, the presence of caries, cracks, and fractures in the tooth structures and open gaps at tooth/restoration interface, which provided pathways for microorganisms and their toxins to diffuse toward the pulp, were the main factors capable of causing damage to this specialized connective tissue (Fig. 7.1a–c).

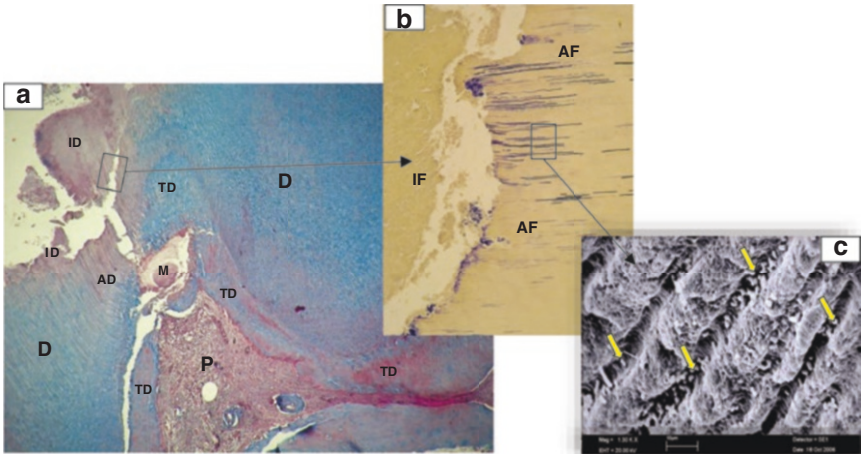

Fig. 7.1 (**a**) Very deep caries lesion in a primary molar that resulted in pulp exposure. *D* dentin; *P* pulp; *TD* tertiary dentin; *M* microabscess; *ID* infected dentin; *AD* affected dentin. Masson's trichrome, 64×. (**b**) Interface between infected and affected dentin. While IF dentin is totally disorganized, the tubular structure of AD is preserved with bacteria displacing through it. Brown and Breann technique, 125×. (**c**) Microorganisms inside dentinal tubules (arrows). Transmission electron microscopy—TEM

7.2 Concepts About In Vitro Animal and Usage/Clinical Tests

Based upon a sequence of laboratory animal and clinical studies performed in the last 30 years, researchers have demonstrated that some dental materials and their components, under specific conditions of use and application, may diffuse across enamel and dentin to cause since a slight tissue inflammation to pulp necrosis. Most of basic investigations performed in this field has focused on the knowledges about molecular biology and mechanisms involved in the process of repair and regeneration of the dentin-pulp complex submitted to various types of aggressions, such as those caused by microorganism contamination, trauma, toxicity of dental materials, and thermal injuries. This has appeared to become more evident and possible by means of the recent advancements in knowledge of the dentin-pulp complex, functions and activities of pulp stem cells, as well as the possibility of developing bioproducts that mimic the extracellular matrix, in which signaling molecules can be added. However, extrapolating this body of knowledge and encouraging scientific data obtained from laboratory and in vivo studies performed in animals to clinical situations has been the most dramatic challenge.

Overall, efforts have been done by researchers to establish dental materials and clinical procedures safe for patients and clinicians as well. In this way, the guideline of international organizations, such as the US Food and Drug Administration (FDA) and International Organization of Standardization (ISO), which determine the performance of rational in vitro trials, in animals and usage/clinical tests, must be followed, and contemporary protocols adapted to present day should be pondered and discussed. Taking into consideration this topic, the main purpose of this chapter is to provide a general and critical view of the relations that permeate the interaction between dental materials and the dentin-pulp complex, as well as establish possibilities of developing new biocompatible products and safe strategies of use capable of benefiting clinicians and patients.

Before discussing the cytotoxic effects and biocompatibility of dental materials, some concepts about in vitro, in animals and usage/clinical tests should be presented. Firstly, we need be aware that the biological effects of dental materials can be evaluated at different research levels, from laboratory to clinical trials. Cell culture assay using in vitro pulp devices is a laboratory methodology that seeks to simulate the role of dentin as barrier to the diffusion of dental material components and as a protein reservoir (Figs. 7.2 and 7.3).

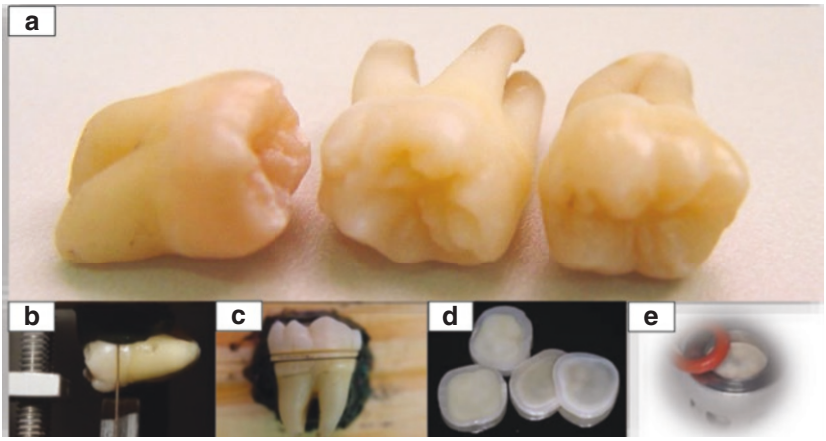

Fig. 7.2 Sequence of procedures to obtain dentin discs. (**a**) Sound third human molars selected; (**b**) after attaching the tooth on a wooden base, the first cut is carried out about 2 mm before the cement-enamel junction; (**c**) second cut 0.5 mm apart from the first cut; (**d**) intact dentin discs selected to be used for indirect test of cytotoxicity; (**e**) dentin disc being adapted to the in vitro pulp chamber

Concerning the in vitro protocols widely used in laboratory, they are considered as sophisticated tests that can assess nearly any aspect of cell function and metabolism, including gene expression, signaling activation, cell cycle and division, inflammatory activation, protein expression, oxidative stress, and many others. Some advantages of the in vitro tests are control of variables, no or minimal ethical concerns, standardization, detailed cell response, reproducible, less expensive, and faster. On the other hand, the main disadvantage of such laboratory tests is that irrespective of the methodology used, the results obtained should be carefully interpreted, and these data cannot be directly transposed to clinical conditions.

7.2.1 Resin Infiltration Systems for Treatment of Enamel White Spot-Like Lesions

Resin infiltration is a micro-invasive treatment for non-cavitated caries management [1]. In this clinical procedure, diffusion barrier is established within the lesion body by using a low-viscosity resin-based material that is capable of blocking cariogenic acid diffusion, arresting the advancement of demineralization and caries progression [2, 3]. It was already shown that the use of resinous infiltrants can mask the opaque look of lesions due to the refractive index of the infiltrant (approximately 1.52) that is similar to that of hydroxyapatite (1.62) [4]. Therefore, after infiltrating the intercrystalline spaces with the low-viscosity resin, the difference in color between the enamel and infiltrated lesion often becomes clinically imperceptible [5]. In this way, resin infiltration systems have been widely employed for esthetic

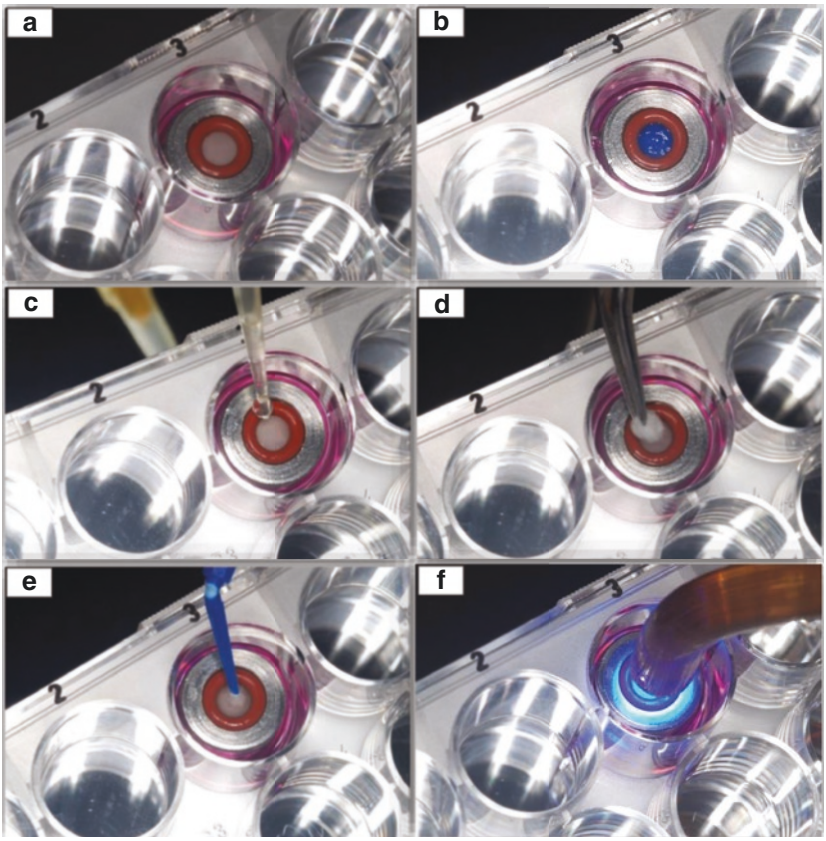

Fig. 7.3 Sequence of application of a etch-and-rinse bonding agent on the occlusal surface of a dentin disc. To simulate clinical conditions, pulp cells were previously seeded on the pulpal surface of the disc. (**a**) Sterilized in vitro pulp device inserted in a well of a 24-well culture plate with the occlusal side of the dentin disc facing up; (**b**) phosphoric acid application on dentin; (**c**) acidic agent carefully rinsed with ultrapure water and simultaneous aspiration of the water to prevent overflow; (**d**) surface drying with absorbent paper; (**e**) bonding agent application; (**f**) bonding agent photoactivation

improvement of developmental defects of enamel, such as fluorosis, traumatic hypocalcification, and molar-incisor hypomineralization [4] (Fig. 7.4).

Overall, the resin infiltration therapy is characterized by a three-step procedure that follows a sequence of application. Firstly, a hydrochloric acid (HCl) agent is used to condition the selected enamel. After rinsing the etched enamel, an ethanol-based drying agent is employed to promote the dehydration of the substrate and improve its wettability. Finally, a low-viscosity resin-based infiltrant containing triethylene glycol dimethacrylate (TEGDMA) is applied and then light-cured (Fig. 7.4). Despite resin infiltrant systems being recommended to be used in specific clinical situations, such as to treat non-cavitated lesions that involve the external

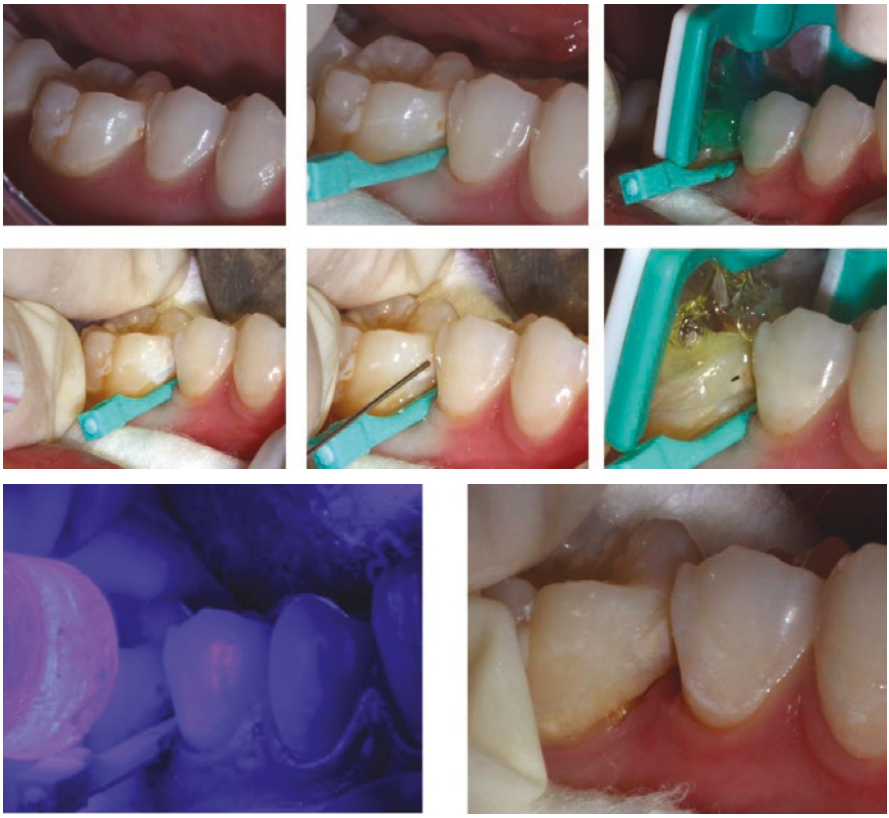

Fig. 7.4 Sequence of a resin infiltration system being used for treatment of enamel white spot caries-like lesion on the mesial surface of a permanent first molar. Courtesy of Prof. Dr. Diego Girotto Bussaneli, Prof. Dr. Manuel Restrepo Restrepo, and Prof. Dr. Rita de Cássia Loiola Cordeiro

third of dentin, their potential adverse effects to the dentin-pulp complex have been little investigated. Even when applied on enamel, it is not yet clear whether TEGDMA released from the products may diffuse through enamel and dentin to reach the pulp cells in toxic concentrations. In a current study, the authors assessed the trans-enamel and trans-dentinal response of odontoblast-like cells and human dental pulp cells after infiltrating enamel white spot-like lesions with the resin infiltration system Icon by DMG (Germany). It was shown that in spite of the buffer action of enamel and dentin, the application of the acidic agent (HCl) on enamel reduced by 70% the viability of pulp cells and upregulated their gene expression of the inflammatory cytokines IL-1β and TNF-α. The authors reported that such pulp cells also had reduced production of total protein, activity of alkaline phosphatase, and formation of mineralized nodules, which are directly related to dentin-pulp repair/regeneration. Based on these data, the authors presumed that HCl was able to diffuse through enamel and dentin to reach the cells in highly toxic concentrations. However, the reduction of cell viability after application of the low-viscosity

resin-based infiltrant to unetched enamel was lower than 30%, which is considered as a non-toxic effect according to international standards [6, 7]. This result seems to indicate that TEGDMA released from the infiltrant agent is not capable of diffusing through the enamel lesion unless the hyper-mineralized surface is removed and interprismatic diffusion channels are created. Another possibility is that the amount of uncured TEGDMA diffused through enamel and dentin was not enough to cause toxic effects to pulp cells. When the resin-based infiltrant was applied to the HCl-etched enamel, the cell's viability reduced by 40%. Interestingly, in this condition, the adverse effects on pulp cells were lower in comparison with HCl agent applied alone to enamel. This finding may be related to the reaction of residual HCl with the monomers present in the resin-based infiltrant. TEGDMA molecules contain ester groups [–C(=O)O–C–], which may undergo hydrolysis by acid catalysis [8]. Therefore, the possible interaction of the acid with the methacrylate esters may justify how infiltrant reduced the toxicity of etching agent by consuming the dissociated HCl and reducing the content of unreacted HCl available for trans-amelodentinal diffusion. Overall, the use of Icon as resin infiltration therapy adversely influenced the metabolic activity of pulp cells. The detrimental side effects were mainly related to the use of HCl. Of course, clinical extrapolations of data obtained from laboratory studies are limited, and further clinical trials as well as investigations using longer periods of evaluation are still needed to determine whether the effects of managing enamel caries lesions with resin infiltration systems are transitory. However, we should be aware that the application of resin infiltration strategies for managing non-cavitated caries lesions, especially if the external third of the dentin is involved, need to be carefully performed.

7.2.2 Silver Diamine Fluoride (SDF)

Among clinical procedures widely used to prevent caries progression, there are those related to minimum intervention, with goals to maintain the integrity of dental tissues, prevent pulp exposure occurrence, and, when necessary, improve the behavior of patients. For example, the atraumatic restorative treatment (ART) and the indirect pulp capping therapy are both considered minimum intervention approaches that employ procedures of selective caries removal in primary and permanent teeth [9, 10] (Fig. 7.5a–c).

Another clinical procedure included in this approach is the application of silver diamine fluoride (SDF) as desensitizing and cariostatic agent [11–13]. Based on its low cost, SDF application has been indicated for blocking caries evolution [14] and preventing radicular caries occurrence in high caries-risk patients [15].

SDF is a salt [$Ag(NH_3)_2F$] that contains fluoride ions (F^-) and silver (Ag^{2+}), which give rise to ammonia complexes (NH_3). When dissolved in water, a highly alkaline and colorless solution is generated [12]. It has been shown that SDH has three specific properties that make it effective to control caries lesion evolution: (1) antibacterial effect, (2) remineralization action, and (3) antiproteolytic activity. All these properties are related with the bioavailability of F^- and Ag^{2+} [13].

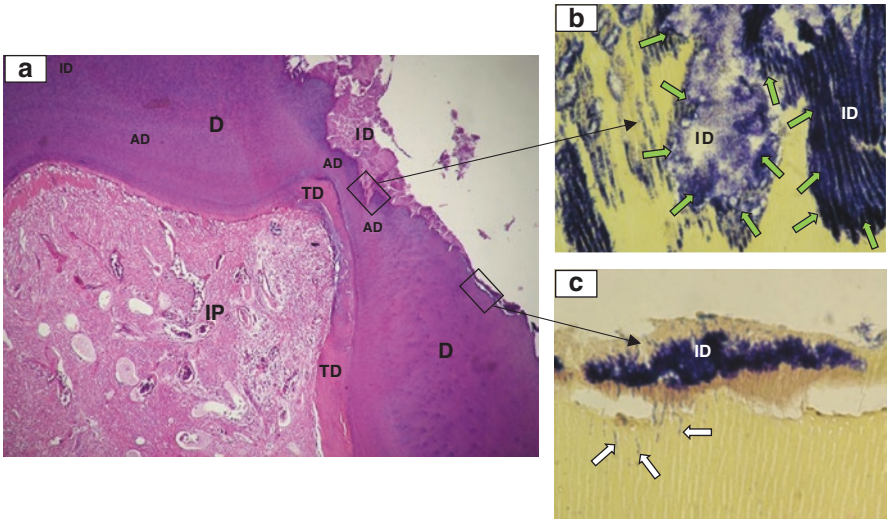

Fig. 7.5 (**a**) Primary molar with very deep caries lesion. *D* dentin; *IP* inflamed pulp; *TD* tertiary dentin; *ID* infected dentin; *AD* affected dentin. H/E, 64×. (**b**) Interface between infected and affected dentin. In the ID zone, wide zones of dentin degradation with high content of bacteria are observed (arrows). Brown & Brenn technique, 125×. (**c**) Note that subjacent to the bacteria-degraded ID, a number of micro-organisms are starting diffusion through dentinal tubules (arrows). Brown & Brenn technique, 180×

Several studies have shown that F^- plays a main role in the process of hard dental tissue remineralization [16, 17]. Additionally, F^- has antimicrobial effects on micro-organisms present in cariogenic biofilm [18]. The chemical reaction between SDF and hydroxyapatite gives rise to silver phosphate and calcium fluoride, which increase the local pH; calcium fluoride also acts as Ca^+ and F^- reservoir, improving the tissue remineralization process [11, 12, 19]. SDF can also deposit mineral along 150 μm of demineralized dentin. The high concentration of calcium and phosphorus deposited by SDF inside dentinal tubules is capable of blocking, even partially, the caries lesion evolution, preventing the occurrence of pulp exposure [20–22]. Previous studies showed that a solution of 38% SDF, which contains 44.800 ppm of F^-, is effective to avoid tooth sensitivity and reduce caries lesion progression [14, 23].

Researchers have shown that SDF has potential to inhibit dentinal endopeptidases, protecting local collagen against enzyme-mediated tissue degradation [11, 23]. The inhibitory activity of SDF on metalloproteinases (MMP-2, -8 e -9) is higher than that caused by sodium fluoride (NaF) and silver nitrate ($AgNO_3$) [24]. The exact mechanism by which such dentin MMPs are inactivated by SDF still remains nuclear. However, based on the fact that dentin MMPs cause degradation of dentin collagen in a neutral pH environment, one may suggest that the high pH of SDF solutions (about 12–13) interferes with these enzymes' activity.

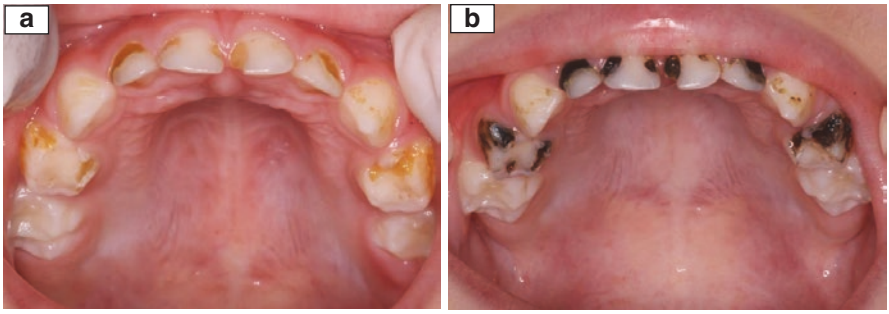

Fig. 7.6 (**a**) Clinical situation in which caries lesions are present in a number of primary teeth. (**b**) One week after performing the topic application of potassium iodide solution, the caries tissue was darkened by impregnation of metallic silver particles generated by oxidation of silver ions released from the cariostatic agent. Courtesy of Dr. Kasandra Verónica Yupanqui-Barrios

When included in the SDF solution, silver ion assumes a remarkable role against biofilm formation, since this specific chemical compound prevents aggregation of *Streptococcus*, *Actinomycetes*, and *Lactobacillus*, which are responsible for the beginning of the caries lesion. Silver ion react with the microorganism's membrane to cause its disruption; in this way, the microorganism's metabolic activity is inhibited [11, 12, 25]. However, it is known that silver ions are oxidated to generate metallic silver, which causes darkening of caries tissue. Therefore, chromatic teeth change seems to be the main clinical adverse effect caused by topic application of SDF on dentin (Fig. 7.6a, b). Despite the darkening of the caries lesion in dentin, the impermeable layer formed on the tissue stabilizes the caries progression [20–22]. It has been demonstrated that the application of potassium iodide (IK) on the SDF-darkened caries lesion may improve the esthetic outcome [26]. This may be explained by the fact that silver ions from SDF interact with IK to form a local white compound, which prevents the darkening of the SDF-treated caries lesion without affecting the positive results caused by this therapy [25, 27].

Only a few data are actually available concerning the cytotoxicity and biocompatibility of SDF and their components to the dentin-pulp complex. On the other hand, after applying SDF 38% solution on caries lesion in dentin, researchers demonstrated that silver ions were present further into the subjacent dentinal tubules [22]. The authors showed that the silver particles released from SDF displaced by around 744.7 μm (±448.7 μm) in dentin. Despite the presence of silver particles inside dentinal tubules, no intense pulp inflammation was observed at 6-month period after using SDF to treat caries lesions present in human teeth [21]. However, it was shown that silver ions were capable of diffusing even 2.490 μm further into dentinal tubules. Therefore, depending on the depth of caries lesion, SDF therapy may allow intense inward dentinal silver ion movement that may reach the pulp chamber in concentrations high enough to cause intense cytotoxic effects. In a previous study, researchers reported that SDF causes severe and persistent damage to

human gingival fibroblasts [28]. Therefore, in order to determine how safe to dentin-pulp complex is the treatment of caries lesions with SDF, laboratory investigations and clinical trials still are needed. In a current study conducted by our research group, standardized dentin discs (0.4 mm thick) were obtained from human molars. These discs were individually adapted into artificial pulp chambers. On the pulpal surface of the discs, odontoblast-like cells were seeded to mimic the odontoblast layer that is physiologically underlying dentin in mammalian (human) teeth. On the occlusal surface of these thin discs, caries lesions were created to simulate a clinical condition of very deep caries in dentin, which was submitted to therapy with Riva Star (SDI, Bayswater, VIC, Australia). Then, after treating the caries lesions with silver diamine fluoride solution (SDF), iodine potassium solution (IK), or SDF followed by IK (SDF + IK) ($n = 8$), the pulp cells were assessed concerning their viability. Considering the non-treated discs as 100% cells viability (control), SDF application on caries lesions decreased the viability of the pulp cells by 46%. On the other hand, IK and SDF + IK reduced cell viability by only 13% and 3%, respectively. These data indicate the positive association of SDF and IK against the transdentinal cytotoxicity of SDF therapy. We all must be aware about the limitations of results of in vitro investigations. However, taking into account the exciting data obtained in this study of cytotoxicity and considering the fact that clinical esthetic outcome can be improved when IK is added to SDF solution, it seems reasonable using these combined components as recommended by the manufacturer (detailed clinical use is presented in Chap. 8).

7.2.3 Tooth Whitening Agents

Tooth whitening is actually the most popular esthetic treatment since it uses a simple and noninvasive clinical technique. The ease of performing the in-office tooth whitening therapy to obtain a relatively fast esthetic results seems to be the main benefit that has made the use of this professional whitening technique the procedure that is still preferred by patients and clinicians. On the other hand, several laboratory studies have shown that whitening gels containing high concentrations of hydrogen peroxide (H_2O_2), such as those used for in-office tooth whitening, induce intense oxidative stress and severe damage to pulp cells [29, 30]. This undesirable adverse effect has been related to the ability of H_2O_2 to disrupt the mineral structure of enamel, which allows trans-amelodentinal diffusion of this toxic reactive oxygen-derived specie (ROS) toward the pulp chamber [31, 32]. The toxicity caused by H_2O_2 to pulp cells seems to be related with post-whitening tooth sensitivity, which has been reported to have more than 70% of patients submitted to this professional esthetic therapy. Recent studies demonstrated that the intensity of the toxic effects of H_2O_2 to pulp cells is inversely proportional to the thickness of tooth enamel/dentin and directly related to concentration and time of application of the whitening gel on teeth [33]. Therefore, the higher the concentration of H_2O_2 in the whitening gel and the longer the time of contact of the product with enamel, the more intense will be the toxicity of the esthetic procedure to pulp cells [34, 35]. Based on these data,

one may suggest that application of in-office whitening gels with 35–40% H_2O_2 for periods of 30–45 min on incisors represents the most dramatic challenge for the dentin-pulp complex. In the last few years, researchers performed clinical investigations, in which in-office tooth whitening was carried out in sound premolars and lower incisors of patients that had their teeth extracted for orthodontic reasons. In these studies, the authors showed that only a slight or no pulp damage occurred in premolars after application of high-concentrated whitening gels for 30–45 min on their buccal surface [36–38]. Almost all premolars submitted to these in-office whitening treatments exhibited normal pulp tissue, and the patients did not report any post-whitening sensitivity. On the other hand, the same professional therapies applied to incisors caused partial necrosis of the coronary pulp associated with local inflammation even two days after concluding the treatment. In these cases, almost all patients reported post-whitening tooth sensitivity (Figs. 7.7 and 7.8a, b).

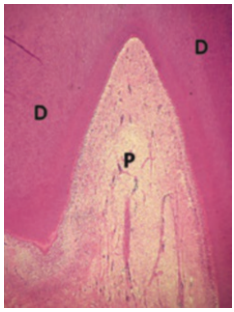

Fig. 7.7 Short magnification of the pulp horn (P) of a human premolar submitted to conventional in-office whitening therapy. The dentin-pulp complex is histologically normal. Below the intact odontoblast layer, which is lining the dentin substrate (D), one can see blood vessels and a number of pulp cells immersed in extracellular matrix. H/E, 64×

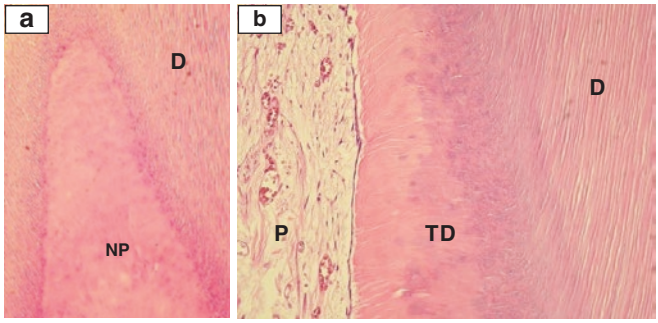

Fig. 7.8 (**a**) Pulp horn of human incisor submitted to conventional in-office whitening therapy. No cells, blood vessels, and extracellular matrix can be observed. Note that this area of the coronary pulp exhibits necrosis (NP). H/E; 96×. (**b**). Radicular pulp of the human incisor submitted to conventional in-office whitening therapy. Intense deposition of tertiary dentin (TD) is observed between the tubular primary dentin and the pulp, which exhibits a number of small dilated and congested blood vessels. H/E, 210×

Based on the results of these clinical studies, in which the whitened teeth were extracted and processed for microscopic analysis of the dentin-pulp complex response against the esthetic therapies, one could consider that the degree of the post-whitening sensitivity was directly related with the intensity of the dentin-pulp damage. In another clinical study, lower incisors from young patients scheduled for extraction were subjected or not to three 15-min applications of a whitening gel with 35% H_2O_2 [39]. Two days thereafter, bleaching effectiveness (according to a value-oriented shade guide) was evaluated, and histological analysis of pulp tissue was performed under light microscope. Immediately and two days after the professional procedure, post-whitening tooth sensitivity experience was recorded. Despite the significant color improvement observed after concluding the esthetic treatments, teeth of all patients experienced post-whitening sensitivity and exhibited significant pulp alterations, characterized by areas of superficial necrosis associated with mild inflammatory reactions. These data were compared to those obtained from elderly patients who also had their lower incisors submitted to the same whitening therapy. Overall, partial pulp necrosis occurred in about 60% of old bleached teeth in comparison with 100% of young teeth. The authors concluded that regardless of the age of patients, the in-office whitening therapy applied to lower incisors causes intense pulp damage, which is related to tooth sensitivity. On the other hand, considering the data of this clinical study, one can suggest that pulp damage is prevalent and more severe in young teeth, which present larger pulp chamber as well as enamel and dentin thinner than old teeth.

Taking into consideration the adverse effects caused by the conventional in-office whitening therapy currently used in dentistry [40], several researchers have evaluated some strategies to minimize them, such as the use of desensitizing agents applied topically or incorporated into the whitening gels. Prescription of analgesics or anti-inflammatories [41] and the application of bleaching gels with low H_2O_2 concentrations [42, 43] have also been assessed and clinically recommended. However, the first two strategies do not prevent H_2O_2 diffusion through the enamel/dentin and consequent pulp damages. Using gels with low H_2O_2 concentrations limits the chromatic change of dental tissues, which makes this treatment unfeasible because it requires several clinical sessions to promote satisfactory whitening outcomes.

Nowadays, the association between the application of ozone (O_3) and whitening gels has shown an attractive strategy to improve the esthetic results and reduce post-whitening tooth sensitivity [44]. Nevertheless, no clinical or laboratory studies have determined the possible toxic effects of this innovative technique to pulp cells. Based upon the knowledge about the mechanisms involved in whitening the mineralized tooth tissues, it would be interesting that all H_2O_2 present in high-concentrated whitening gels could interact with the chromophores in order to prevent residual H_2O_2 from reaching the pulp tissue. However, the high concentration of H_2O_2 in gels frequently used for professional tooth whitening and low oxidation capacity of this toxic molecule allow residual H_2O_2 to remain in dentin (free-H_2O_2) to diffuse quickly toward the pulp chamber. Therefore, other exciting approach that has

actually been widely investigated is incorporating catalyzing agents in whitening gels with variable concentrations, which may result in a similar esthetic efficacy to that obtained with conventional in-office tooth whitening [45, 46]. This strategy basically has the objective of accelerating the decomposition of residual H_2O_2 present in the whitening gels by the catalyzing agent, which induces the generation of other highly reactive oxygen species (ROS) with an extremely short half-life [31]. Consequently, after interacting and causing very fast degradation of the chromophores present in darkened dental tissues, the new ROS generated are eliminated, reducing the possibility of trans-amelodentinal toxic effects to pulp cells [47, 48]. To make this innovative strategy viable, researchers started evaluating the use of transition metals and enzymes with catalyst potential, associated or not with the photocatalysis of whitening gels with LED at a visible violet wavelength (V-LED) [45]. The use of V-LED for tooth whitening has also been justified by the fact that the V-LED wavelength (405–410 nm) corresponds to the absorption peak of chromophores. Considering that these colored organic molecules are highly reactive, it is assumed that the presence of violet light could trigger the instability and rupture of chemical bonds, promoting the bleaching effect by a photophysical process. Based on the potential benefits of the chemical catalysis and photocatalysis of H_2O_2 to professional tooth whitening, our research group evaluated the influence of the association of manganese oxide (MnO_2) and V-LED on the esthetic efficacy and trans-amelodentinal cytotoxicity of whitening gels with 6% and 10% H_2O_2. In this specific investigation, we showed that associating LEDv+MnO_2 in whitening procedures with gels containing such low H_2O_2 concentrations results in esthetic outcome similar to that obtained with the conventional in-office tooth whitening, in which a gel with 35% H_2O_2 was used. Compared to professional whitening, we demonstrated that the lowest indices of trans-amelodentinal H_2O_2 diffusion occurred when both low-concentrated whitening gels containing MnO_2 were irradiated with V-LED. Taking into consideration this fact, we observed that the chemical catalysis of the H_2O_2 present in the whitening gels with MnO_2 and their photocatalysis with V-LED caused only a discrete toxicity to pulp cells. On the other hand, the conventional in-office whitening therapy caused an intense oxidative stress and damage to pulp cells. Recovering the enamel with a polymeric catalyst primer before applying the whitening gel, which is then submitted to V-LED photocatalysis, is another approach that has shown excellent results. Despite these exciting findings that have established more effective and biocompatible whitening approaches to dentin-pulp complex, further investigations are still needed. However, all the innovative strategies presented here have driven the future of tooth whitening therapies, especially for professional treatments. Thus, taking into consideration the scientific data currently available, we must be aware that the conventional in-office whitening therapies widely used nowadays are extremely toxic to pulp cells and may cause post-whitening tooth discomfort to patients. Additionally, one should pay attention to the fact that pulp damage caused by these professional whitening therapies seems to be more intense in teeth of young patients.

7.2.4 Bonding Agents, Glass Ionomer, and Calcium Silicate Cements

For several decades, the development of adhesive dental materials has revolutionized many aspects of restorative and preventive dentistry, in such way that procedures toward cavity preparations were revisited in order to establish the successful minimal-invasive dentistry. The clinical use of adhesive materials improved the esthetic outcomes and reduced microleakage at the restorative material-tooth interface, decreasing postoperative sensitivity, marginal staining, and consequently secondary caries. Bonding agents, which made the resin dental substrate interaction achievable, are solutions of resin monomers that contain hydrophilic and hydrophobic groups as well as curing initiators, inhibitors or stabilizers, solvents, and, in some cases, inorganic fillers in their composition. Disregarding the clinical technique of application of these resin-based dental materials, they were developed specially to bond enamel, dentin, amalgam, metal, and porcelain. The important properties of bonding agents have given clinicians the option of using them for various dental treatments and application procedures. Beside allowing repair of deteriorated or deboned restorations, the use of bonding agents improves distribution of functional stress at tooth structure and restorative materials in such way that the weakened tooth structure is protected and reinforced. Bonding agents may be applied directly on smear layer, by dissolving it or incorporating it into the bonding process. These resinous materials may also be applied directly on dentin; in this case, the smear layer is previously removed from dentin by acid etching. Different chemical compositions of bonding agents and their variable sequence of application on dentin substrate have given rise to diverse resin-dentin interface features and shear bond strength values, as well as influenced the hybrid layer degradation with time. Bonding agents applied on dentin result in hybrid layer of variable thicknesses and short or long resin tags formation into dentinal tubules that frequently are related with displacement of resin components through dentinal tubules.

Several studies have shown that resin monomers widely found in bonding agents, such as HEMA and TEG-DMA, have defined toxicity to pulp cells [49, 50]. Therefore, taking into consideration the fact that when resins are light-cured, only 55–60% of the monomers react, researchers demonstrated that transdentinal inward diffusion of uncured monomers occurs; these phenomena are inversely proportional to the remaining dentin thickness (RDT) between the cavity floor and pulp tissue. In a clinical study, the authors applied an etch-and-rinse bonding agent in deep cavities prepared in premolars indicated to be extracted for orthodontic reason [51]. One month after concluding the adhesive restorations, the microscopic analysis of the dentin-pulp response against the clinical procedures was carried out. The authors showed that when the RDT was thinner than 300 μm, inflammation and disorganization of pulp tissue occurred. These histological findings were related to long resin tag formation and resin monomer diffusion through dentinal tubules (Figs. 7.9a–c and 7.10).

When the cavity floor was lined with a biocompatible dental material (hard-setting calcium hydroxide cement) before adhesive restoration of the cavities, no pulp damage was observed. It was also demonstrated that disregarding the intensity

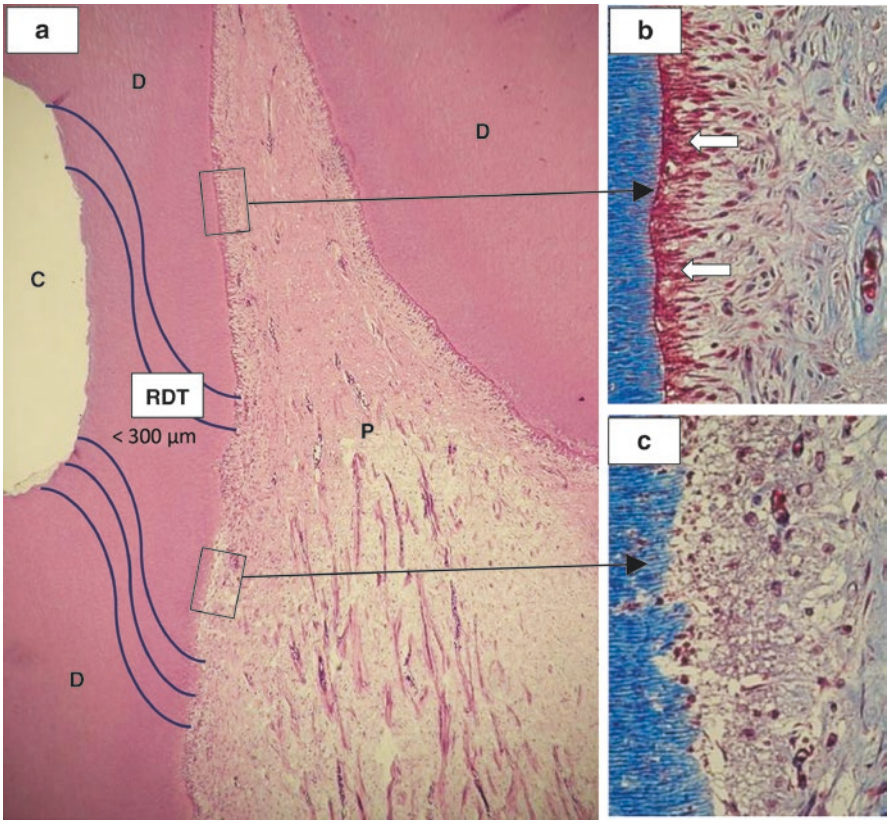

Fig. 7.9 (**a**) Class V cavity prepared in human tooth. The blue lines represent the dentinal tubules away from the cavity floor to the pulp. *C* cavity; *D* dentin; *P* pulp; *RDT* remaining dentin thickness <300 µm. H/E, 32×. (**b**) High magnification of the area selected in (**a**). The monolayer of odontoblasts is preserved (arrows). The subjacent pulp tissue exhibits normal histological characteristics. Masson's trichrome, 125×. (**c**) High magnification of the area selected in (**a**). Note that the odontoblast layer is completely disrupted and some cells aspirated into dentinal tubules. The subjacent pulp tissue is disorganized and presents inflammatory mononuclear cells. Masson's trichrome, 125×

of the damage presented by the pulp tissue, all patients did not claim any postoperative tooth sensitivity. In another similar study, researchers applied a self-etching bonding agent in deep cavities prepared in human premolars [51, 52]. The authors observed lower and shorter formation of resin tags, as well as lighter inward displacement of uncured resin globules through dentinal tubules in comparison with the etch-and-rinse bonding agent. However, the amount of resin components that reached the pulp was enough to cause disruption of the odontoblast layer, inflammatory response, and local proliferation/dilatation of blood vessels. When bonding agents were applied on human pulps mechanically exposed [52], the resinous material elicited a chronic inflammatory pulp reaction mediated by macrophages and giant cells, which appeared engulfing particles of uncured resin displaced into the

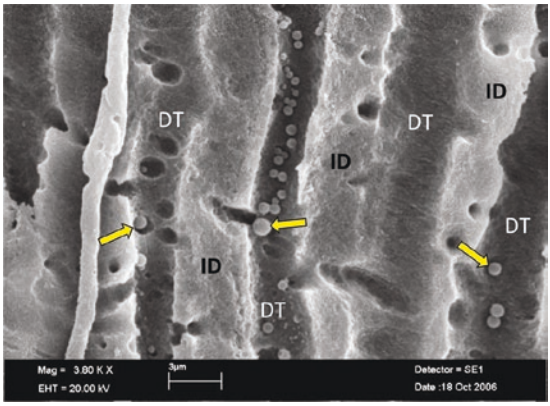

Fig. 7.10 This image shows a number of uncured resin globules (arrows) displaced into dentinal tubules. *DT* dentinal tubule; *ID* intertubular dentin. MEV

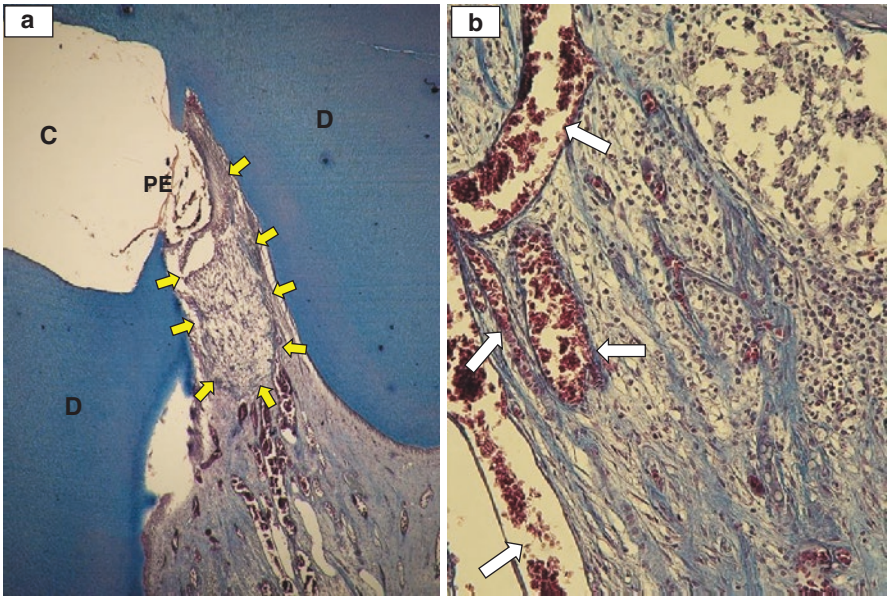

Fig. 7.11 (**a**) After very deep cavity preparation, the pulp tissue was carefully exposed, acid etched, and then capped with a boning agent. *C* cavity; *D* dentin; *PE* pulp exposure; *Arrows* uncured resin released from the bonding agent. Masson's trichrome, 32×. (**b**) Bonding agent components displaced into the pulp triggered an intense inflammatory response at distance of the pulpal wound. Note that the inflammatory reaction is characterized by a number of mononuclear cells, degradation of extracellular matrix, and proliferation of dilated and congested blood vessels (arrows). Masson's trichrome, 210×

pulp (Fig. 7.11). This persistent tissue inflammation that did not allow odontoblast-like cell differentiation and complete dentin-pulp regeneration at the pulp exposure site even 300 days after the clinical procedure resulted in inner-dentin resorption. On the other hand, when calcium hydroxide was used as capping agent, hard barrier formation was deposited by new differentiated odontoblast-like cells (Fig. 7.12).

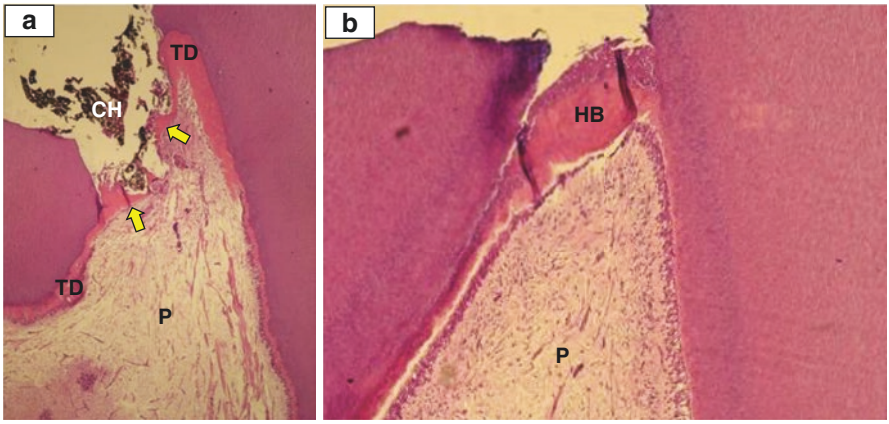

Fig. 7.12 (**a**) Calcium hydroxide (CH) applied on a pulp exposure performed in human tooth, which was extracted after a few days. Note the deposition of tertiary dentin (TD) and the partial formation of hard barrier (arrows) adjacent to the capping agent. H/E, 32×. (**b**) With time, a thick defined hard barrier (HB) is formed at the pulp exposure site. Note the new layer of differentiated odontoblast-like cells underlying the HB. The subjacent pulp tissue (P) exhibits histological characteristics of normality. H/E, 125×

A sequence of clinical/histopathologic studies performed in human teeth, in which different bonding agents were applied in very deep cavities or used as capping agents, demonstrated similar disastrous pulp results. On the other hand, when the cavity floor was lined with hard-setting calcium hydroxide cements (CHC) or different formulations of glass-ionomer cements (GIC) before proceeding the adhesive restoration, mild or no pulp damage was observed [53–57]. These clinical/histopathologic studies also performed in human teeth demonstrated that most of these cements can be recommended for clinical situations in which a layer of sound or affected dentin remains between the cavity floor and the pulp (Fig. 7.13).

In a few years ago, researchers applied two resin-modified GICs – Vitremer and Vitrebond on the floor of deep cavities prepared in human teeth [55]. However, before using Vitremer, the dentin substrate was pretreated with a primer (polyacrylic acid plus 2-hydroxyethyl methacrylate) such as recommended by the manufacturer. Teeth were extracted after 7 or 30 days and processed for microscopic evaluation. The authors observed that Vitremer specimens exhibited diffusion of uncured monomers across dentinal tubules associated with damage to pulp cells and inner resorption of dentin. On the other hand, no pulp damage was observed for Vitrebond specimens. The notable biocompatibility of the conventional powder/liquid form of Vitrebond was also demonstrated in several other studies performed in human teeth. Conversely, in spite of being considered biocompatible, the paste/liquid formulation of this cement (Vitrebond Plus Light Cure Glass Ionomer Liner/Base), which was developed and introduced to the market in convenient dispensing "clicker" device with the aim of facilitating handling and shortening the clinical time, caused more damage to the pulp than the conventional version [54]. In another study, researchers assessed the response of human pulps after using a conventional GIC (Riva

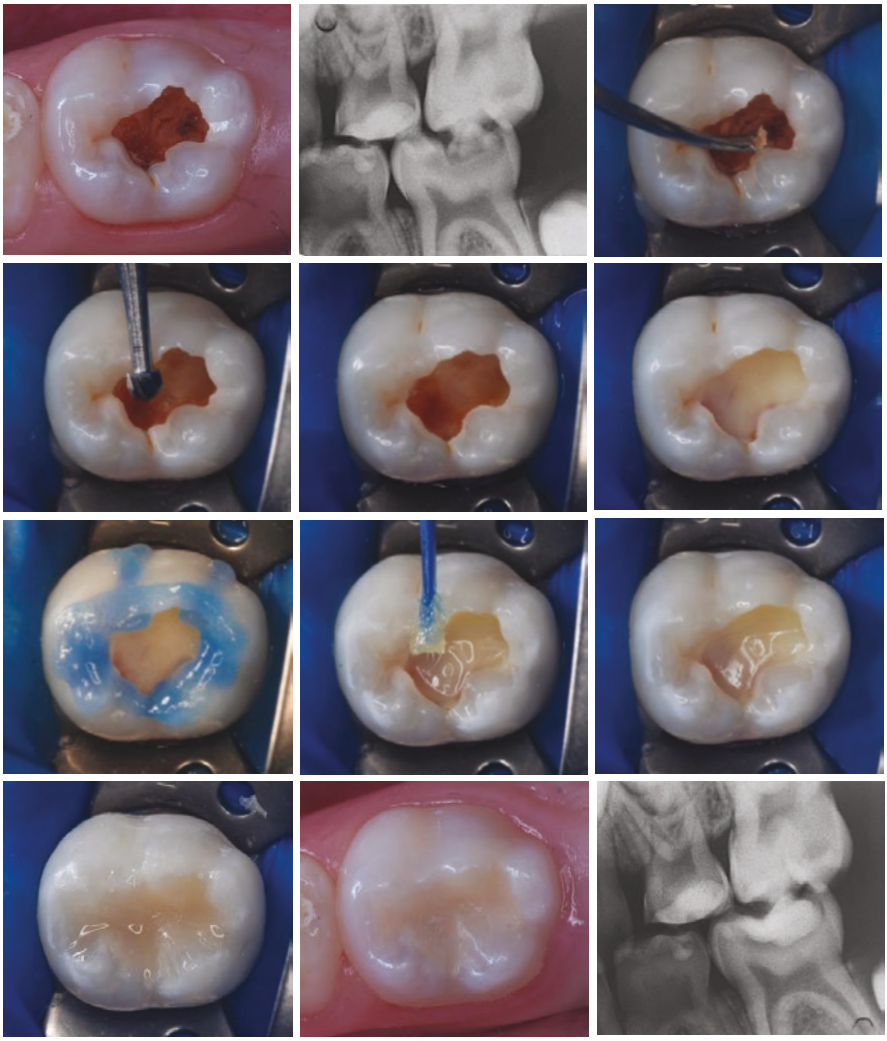

Fig. 7.13 Sequence of adhesive restoration of a cavity following selective caries removal. After lining the cavity floor (affected dentin) with the resin-modified glass-ionomer cement Vitrebond™, the lateral walls and enamel were conditioned with acidic agent. Finally, the bonding agent was applied as recommended by the manufacturer and the composite resin used to fill the cavity

Self-Cure) or a resin-modified GIC (Riva Light-Cure) to line very deep cavities prepared in human teeth [56, 57]. Although both cements were considered biocompatible for such clinical application, Riva Light Cure was more toxic to pulp cells than Riva Self-Cure. In all these studies performed in human teeth, no postoperative tooth sensitivity was reported by the patients, which might mistakenly indicate that all ionomeric cements do not cause any damage to pulp tissue. Actually, we have recommended lining deep cavity floors with resin-modified GICs rather than

different formulations of CHC. This is because resin-modified GICs have several important properties such as fluoride release, adequate flexural and diametral tensile strength, elastic coefficient of thermal expansion and modulus of elasticity similar to dentin, as well as chemical adhesion to both enamel and dentin, which are not presented by all CHC formulations. However, based on the reliable body of scientific data established by a number of well-conducted laboratory and clinical/histopathologic trials, the most appropriate resin-modified GIC must be carefully selected to be used in specific clinical situation to preserve the dentin-pulp complex health.

When pulp exposures mechanically created in human teeth were directly capped with a resin-modified glass-ionomer cement, a wide displacement of uncured resin and globules of glass occurred [57]. In this condition, the elicited chronic inflammatory response did not allow regeneration of the dentin-pulp complex even after almost 1 year after performing the clinical procedure. In this way, rather than resin-based materials, biocompatible dental products capable of stimulating dentin-pulp regeneration should be used as capping agent.

The calcium silicate cements—Mineral trioxide aggregate (MTA) and Biodentine, as well as specific formulations of calcium hydroxide—have been recommended as capping agents. MTA and Biodentine present similar mechanism of action, which is based on the release of calcium hydroxide and hydrated calcium silicate, increasing the pH at the pulp wound site. Concerning primary teeth, these biocompatible materials have been indicated for pulpotomy in specific clinical situations of extensive caries and pulp exposures but with no evidence of radicular pathology. Although formocresol still has been considered the gold standard material for pulpotomy treatments in primary teeth, MTA and Biodentine have demonstrated excellent performance and high clinical/radiographic success rates [58]. This is because they are able to maintain teeth integrity and preserve pulp vitality, allowing phonation, esthetics, and masticatory function until exfoliation time [59, 60]. Despite the most of investigations performed in human teeth using MTA or Biodentine as capping agents evaluates the clinical and radiographic success rates, only a few of them has carried out microscopic analysis of the dentin-pulp complex response against these calcium silicate cements. Many years ago, researchers applied MTA directly on pulp exposure performed in premolars of young patients, and the teeth were extracted for microscopic analysis of the dentin–pulp complex [61, 62]. At short-time evaluation, the authors demonstrated that components released from MTA displaced into the coronal pulp. With time, these MTA components were observed in endothelial cells and inside pulp blood vessels. These data should be carefully interpretated since dental materials components inside blood vessels may result in embolism, which seems to be a risk for patients' health. Considering the fact that there is not a sufficient scientific evidence to certify the safety of clinical application of Biodentine and new formulations of MTA on pulp exposures, the use of such calcium silicate cements as capping agent must be discussed at this time. New biological approaches based on the application of tissue engineering knowledge associating scaffolds, bioactive molecules and stem cells for regeneration of the dentin-pulp complex have been assessed in the last decades [63–65]. In this way, researchers have worked hard to develop and improve innovative pulp-capping biomaterials capable of driving the regeneration of

the dentin-pulp complex mediated by resident stem cells. In a current study, chitosan scaffolds capable of releasing bioactive concentrations of simvastatin was prepared and assessed with the objective of developing a cell-free tissue engineering system to be employed for pulp-dentin regeneration [63, 64]. Instead of causing an immediate superficial necrosis to pulp cells, as observed when materials with high pH, such as calcium hydroxide and calcium silicate cements, are used as capping agents, the new simvastatin-loaded scaffold increased the chemotaxis and regenerative potential of pulp cells. When small concentrations of calcium were added to simvastatin-loaded scaffold, the experimental biomaterial created a microenvironment capable of attracting pulp cells to its surface and inducing the overexpression of odontoblastic markers in a cell-homing strategy [64, 65]. Overall, rather than using synthetic dental materials on pulp exposures that may have some adverse effects to resident stem cells, more biological approaches have driven and improved the contemporary regenerative dentistry.

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SDF as an Adjunct Approach for the Management of Caries

8

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Contents

8.1 Introduction

Silver was known to have antibacterial properties since antiquity and has been used for over a century in medicine as an antibacterial agent and to treat wounds and burns [1].

In dentistry, silver has been used since the early 1900s for the management of dental caries in different compounds, mainly as silver nitrate and Howe's potion (ammoniacal silver nitrate). The use of such compounds was advocated for the

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sterilization of infected dentin in deep caries lesions rather than mechanical removal by bur or spoon with possible exposure and injury to the pulp [2].

More recently, silver has regained interest to treat dental caries in a minimally invasive or nonsurgical manner. This has been popularized since the advent of silver fluoride and silver diamine fluoride in different concentrations and preparations that have been designed for different specific purposes: from disinfection of a lesion prior to restoration, with the aim of dentin desensitization to caries arrest with and without removal of carious tissues.

Silver diamine fluoride (SDF) was developed in Japan in 1969 as an agent for caries arrest [3], and it was prepared as a clear liquid containing high concentrations of silver as an antibacterial agent and fluoride as a remineralizing agent, stabilized in an ammonia solution. Since then, many products with different concentrations and indications have been introduced to the market in many countries, and their use has been growing as an addition or an alternative to traditional restorative treatment. In the United States, SDF at a 38% concentration was approved by the Food and Drug Administration (FDA) in 2014 as a dentin desensitizing agent for patients over 21 years of age. Many clinical trials all over the globe have reported the success of different concentrations used for caries arrest [4], and the American Academy of Pediatric Dentistry (AAPD) issued a guideline in 2017 supporting its off-label use for caries arrest in primary teeth as part of a comprehensive caries management program [5]. The American Dental Association (ADA) followed in 2018, supporting the use of SDF over fluoride varnish for the arrest of cavitated coronal lesions [6].

8.2 SDF'S Use for Caries Arrest

SDF has gained popularity as an alternative to traditional restorative treatment because it is relatively easy to apply. It does not require removal of carious tissue to achieve caries arrest [7]; therefore, it doesn't require the use of local anesthesia or rotary instruments. It is relatively inexpensive and can be applied in many settings because it does not require complex instruments or tools. It also poses minimal risks, which has been confirmed in numerous clinical trials in preschool children conducted all over the world, which have not reported any major or significant complications from its use [4].

Clinical trials report arrest rates with SDF that range from 40% to 95% [8, 9]. Caries arrest is typically diagnosed when black staining and hardness of the surface of the lesion are achieved, and the extent of the lesion stops its progression. Time to arrest the lesion and sustained arrest depend on the concentration of the product (12%, 30%, or 38%), frequency of application (once vs. twice a year), location of the caries lesion in the mouth (anterior vs. posterior teeth), the location of the caries lesion on the tooth (buccal, lingual, proximal, or occlusal), the effectiveness of plaque removal after application, and the challenge of the dietary patterns of the individual (frequency of exposure to cariogenic foods and beverages) [10, 11]. To achieve caries arrest in cavitated dentin lesions, 38% SDF concentration is more effective than lower concentrations, and application twice a year is more effective

than once a year [10]. A study that reported the arrest rates by area of dentition using 38% SDF twice a year stated that lower anterior teeth had 92% arrested lesions, maxillary anterior teeth 86%, lower posterior teeth 62%, and maxillary posterior teeth only 57% [11]. Occlusal surfaces required a longer time than buccal or lingual surfaces to achieve caries arrest [10, 11]. Children that had a higher visible plaque index score had a lower chance to have their caries arrested, [11] and children who had more than three snacks or three times milk per day presented lower rates of arrest [9]. For all these reasons, it is obvious that SDF does not work optimally as an isolated therapy, but it yields best results when used in conjunction with a comprehensive plan for caries management that includes methods to reduce the cariogenic challenge through plaque control and diet education. This is also very important because SDF is contraindicated in teeth that are pulpally involved. Therefore, in a comprehensive treatment plan for a child that may have pulpally involved teeth, the appropriate pulp treatment and subsequent restoration or surgical removal must be considered and planned according to the child's expected cooperation for treatment.

In addition to the characteristic black staining of treated lesions, SDF's side effects include a metallic taste immediately after application and gingival irritation in some cases, especially when using products with higher pH. For this reason, SDF's use is contraindicated in patients who have silver allergies or who may have stomatitis or ulcerative gingival lesions.

Although caries arrest with SDF is very effective for cavitated dentinal lesions, several studies have shown that for the arrest of enamel lesions only, 5% sodium fluoride varnish has similar effectiveness 10, [12]. One of the beneficial effects of SDF is the immediate desensitization of dentinal tissues where it is applied. This can be very helpful in the clinical management of caries especially with patients who present with sensitive areas that prevent them from establishing an effective oral hygiene routine.

8.3 Appearance and Clinical Application

SDF 38% as marketed in the USA, is a clear/blue liquid with metallic taste that comes in a dropper bottle or in unit-dose ampules. One drop typically treats 4–6 lesions (depending on the size), and although the cost per lesion varies with the individual product, the approximate cost per drop is US $1.

A sign of caries arrest is the dark staining of the decayed enamel and dentin. Although sound enamel does not discolor, any areas of demineralized enamel treated will also look black after SDF application (see Fig. 8.1a, b). Staining can be more or less noticeable depending on the location of the cavities and the demineralized areas that can come in contact with SDF during application. This characteristic staining may pose esthetic concerns and can be a deterrent for its use.

A study that evaluated parental perception and acceptance of SDF's staining effects of parents from diverse backgrounds in New York City's metropolitan area found that parents found the use of SDF to be more acceptable on posterior regions

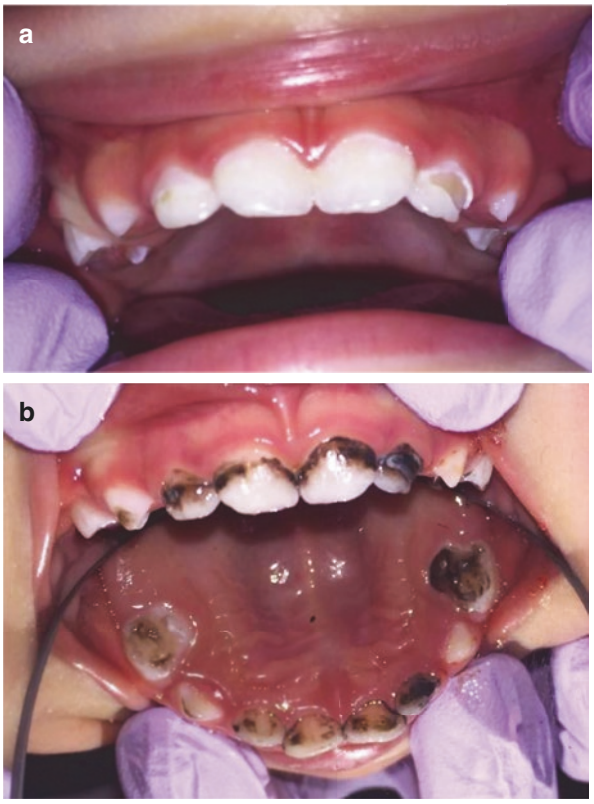

Fig. 8.1 (**a**) Cavitated and non-cavitated lesions before SDF treatment; (**b**) caries lesions in enamel and dentin (cavitated and non-cavitated) with typical SDF staining

than on anterior regions where the black staining is visible. However, many parents would allow for its use if it deferred or avoided more advanced forms of behavior management to deliver treatment (like sedation or general anesthesia), which suggests that many parents are open to compromising esthetics in favor of using a less invasive approach for caries management. Even then, 40% of parents found the treatment unacceptable under any circumstance on anterior teeth and 30% on posterior teeth. Acceptability for treatment varied according to the parent's educational and economic status. For these reasons, the study recommends that to identify parents who would be dissatisfied with the esthetic results, a thorough informed consent with realistic photographs of treated teeth should be presented and discussed [13, 14].

The use of potassium iodide (KI) after SDF or silver fluoride application was introduced to remove excess ionized silver and eliminate or reduce the severity of the staining [15]. Riva Star (SDI Limited. Victoria, Australia) developed a product primarily marketed for dentin desensitization with KI to follow the SDF, or silver fluoride application. The effectiveness of SDF for caries arrest when used together with staining reduction by KI is limited. Results from a clinical trial using this technique to reduce the staining after SDF or silver fluoride application for caries arrest

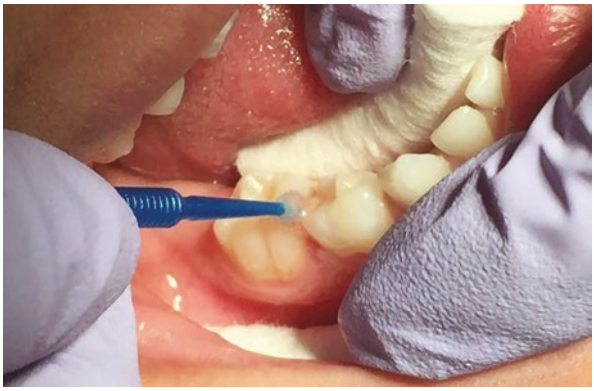

Fig. 8.2 SDF application

in children report that lesions treated with KI after SDF or silver fluoride were less likely to remain arrested [16].

SDF will also stain skin (temporarily) and other surfaces it comes in touch with, so it must be handled with care. For its application, one should use the following steps [17]:

- Dispense 1 drop for 4–6 teeth on a glass dappen dish.
- Clean the caries lesions thoroughly with a toothbrush.
- Place Vaseline on lips.
- Isolate with cotton rolls.
- Apply SDF with microbrush to caries lesion, and rub gently for 1 min (Fig. 8.2).
- Allow to air-dry.

Because the caries arrest varies depending on the size and location of the cavity, it is recommended to bring back the patient 1–2 weeks later to confirm total arrest and re-apply SDF if necessary. This is especially important when treating lesions in posterior teeth, where the rates of arrest are lower with a single application [5].

8.4 SDF'S Mechanism of Action in Enamel and Dentin

The chemical formula for the SDF solution is $[Ag(NH_3)_2]F$, which consists of silver diamine complex and fluoride ions [18], which are stabilized in an alkaline solution. There are at least eight commercially available 38% SDF solutions across the world [19], and the reported concentrations of silver are in the range of 248,000 to 287,000 ppm and 44,333 to 60,022 ppm for fluoride [18–21]. The pH of 38% SDF solution is in the range of 9.1 to 10.0 in most commercial preparations. Products with a higher pH would produce more gingival irritation when applied without a rubber dam. The short-term stability of silver and fluoride ion concentrations seems to be stable over 28 days [18, 22] for most products, but some seem to be out of the range [19, 20]. Patel et al. reported that some products had much higher measured

concentrations for silver and fluoride that were at least 25% higher than the expected concentration. So, it is recommended that clinicians use products that have been tested by independent laboratories.

Silver in SDF has antibacterial effects [23]. In vitro studies report that the antibacterial effects of silver ions on cariogenic bacteria like *Streptococcus mutans* could be a result of the following three activities:

1. The ability to disrupt the bacterial cell wall structure through binding with disulfide anions in the protein membrane, which allows easy penetration through this membrane.
2. Inhibition of DNA replication of bacteria through attaching to DNA's guanine component.
3. Cytoplasmic enzyme denaturation by binding to sulfhydryl (thiol) groups of cysteine, which interferes with the activity of essential enzymes [24] and bacterial metabolism, inhibiting bacterial growth.

Silver also seems to inhibit collagen degradation by inhibiting cathepsins, and the by-products of its precipitation may contribute to the rehardening of dentin [25]. However, many of the statements on SDF's actions on bacterial communities have been reached by studies conducted using in vitro biofilm models with single or selected species combinations, when the oral microbiome involves at least 600 species with complex interactions among them. Few studies have been conducted to be able to elucidate the real action of SDF on bacterial communities within the dentin where it is applied, in adjacent surfaces of the tooth, and its action on the whole oral microbiome. Current studies have not been able to find significant microbial changes in children with active caries following SDF applications and those with caries arrested by SDF when testing plaque samples [26, 27]. Another recent study reported that although they did not detect any changes in the microbial distribution in the surface biofilm of SDF treated lesions, they found significant changes in the microbiota of excavated subsurface dentin of SDF treated lesions, observing a healthier community composition in the SDF treated dentin. Based on their findings, they suggest that SDF's antibacterial actions happen in the deeper region of the lesion, ultimately arresting caries progression [28].

The high concentration of fluoride in SDF acts as a remineralizing agent, strengthening enamel and dentin by forming fluorohydroxyapatite crystals. Remineralized enamel and dentine crystals are less soluble to further acid attack, which is also manifested in increased hardness of the tissue. The increase in levels of calcium and phosphate in the surface layer of the arrested dentin caries lesion after SDF treatment also results in increased microhardness [28]. Fluoride also inhibits collagen degradation in dentin by inhibiting matrix metalloproteinases activity. It is also proposed that silver and fluoride in alkaline solution have a synergistic effect that seems to create an unfavorable environment for collagen enzyme activation, therefore reducing dentin degradation [23, 25].

In terms of SDF penetration into the dental tissues, Li et al. in 2019 [29] used scanning electron microscopy energy-dispersive X-ray spectroscopy (SEM-EDS) to study silver penetration and precipitation in enamel and dentin. Their results show that silver penetrates into both demineralized enamel rods (even without cavitation) and dentinal tubules, and the degree of silver penetration was positively related to the degree of enamel and dentin demineralization. They suggested that silver oxide, silver sulfide, and/ or silver phosphate could be the main culprits of the black stain on the surface of treated carious lesions and that penetration and precipitation of silver in treated carious lesion can reach depths of approximately 2500 μm, which can reach the dental pulp tissue [29]. Using similar methodology, Sulyanto et al. in 2021 observed that after SDF application, multiple dentinal tubules were occluded by silver, while some others were occluded by calcium phosphate [30].

8.5 SDF on the Pulp Complex

Other chapters have described the changes that occur in pulpal tissues since the very early stages of bacterial invasion of the dentin and the changes that are elicited in the pulp when different materials are applied to open dentinal tubules. Therefore, it is expected that regardless of the aim for which SDF is used (desensitization or caries arrest), it is going to have very specific responses from the pulpal tissue, perhaps depending on the depth of the lesion to which it is applied, its mineral loss, and the proximity to pulp cells.

It has been reported since early studies that direct application of silver compounds directly on the pulp causes pulp necrosis [2, 31], but few recent studies report the effects of SDF on the pulp when it is applied on dentin. One study applied SDF to cavities prepared on virgin premolars scheduled for orthodontic extractions and compared the pulpal effect to glass ionomer cement (GIC), calcium hydroxide, and no treatment control [32]. Premolars were extracted 6 weeks later, and histological examination was done. No inflammatory changes were observed in any of the groups, and significantly more specimens in the SDF and GIC groups showed tertiary dentin deposition (TDD) when compared to the control group. The study demonstrated the TDD-inducing ability of SDF and Type VII GIC and also established their biocompatibility when used as IPT materials [32]. But this study was done on sound teeth (with no previous pulpal reaction to the carious process), and changes were only assessed at 6 weeks.

Another case report describes the histological characteristics of a primary tooth with deep caries in proximity to the pulp after 6 months treatment with SDF, which was extracted when it was deemed to be non-restorable [33]. Their light microscopy observations revealed no carious pulp exposure, evidence of tertiary dentin formation, and minimal pulp inflammation. An intact but flattened odontoblastic layer was found adjacent to the irregular tertiary dentin, dentinal tubules with silver deposits to a depth of 1 mm, and no visible bacteria. They conclude that SDF leads

to histologic changes that prevent pain and pulp deterioration and most likely facilitate pulp healing [33]. It is important to stress that this is a report from a single specimen, and the observations with light microscopy are limited in terms of identification of silver deposition in pulp tissues with no possible visible staining. Additionally, identification of bacteria at 20× magnification with hematoxylin and eosin stain would be very limited.

Another ex vivo study reported the findings on the pulp complex of eight primary teeth with dentin-enamel caries. The teeth were extracted after 1 year of SDF application [34]. Scanning electron microscopy (SEM) showed areas of hypermineralization in the intertubular dentin and few blocked tubules, while energy-dispersive X-ray detector (EDS) done on only one sample detected the presence of silver in the center of the lesion, and its concentration declining at the edges, with no silver observable in the areas farthest from the lesion. Bright-field optical microscopy (OM) showed SDF sealing the tubules only in the surfaces where it was applied, with limited penetration beneath. The tubules appeared normal, and the pulp tissue under treated areas showed chronic inflammatory infiltrate and formation of tertiary dentin, with no silver precipitation. From their observations using the different techniques, they concluded that SDF causes minimal adverse effects on pulpal tissues.

Another ex vivo study done by Sulyanto et al. in 2021 confirms the formation of tertiary dentin regions located around and inside the pulp chamber, with thicker tertiary dentin in teeth treated with SDF over longer periods of time [30].

A recent systematic review was performed specifically to collect all published data on the pulp response to SDF up to 2021 [35] and found only five publications that dealt specifically with this theme (including the first three described above). Grouping the results of these three studies with additional animal studies, they comprised data from a total of 30 teeth and reported that indirect SDF application caused none or only mild inflammatory response of dental pulp, with odontoblasts showing increased cellular activity. Tertiary dentin was formed in the pulpal side of the cavity with indirect SDF application, with accentuated incremental lines of tertiary dentin reflecting disturbances in mineralization. Silver ions were found to penetrate along the dentinal tubules but were not detected inside the pulp in most studies. They concluded that SDF application directly onto pulp tissue causes pulp necrosis but that indirect SDF application (to carious dentin) is generally biocompatible, causing only a mild inflammatory response, increased odontoblastic activity, and increased tertiary dentin formation.

The results of all of these studies indicate that as long as the pulp tissue is still vital, when SDF is placed on dentin, even without caries removal, its remineralizing actions harden the dentin and block dentinal tubules, and the antibacterial effects reduce or eliminate bacteria in the remaining dentin, allowing the pulp to heal and produce tertiary dentin to further seal against the bacterial invasion (Fig. 8.3).

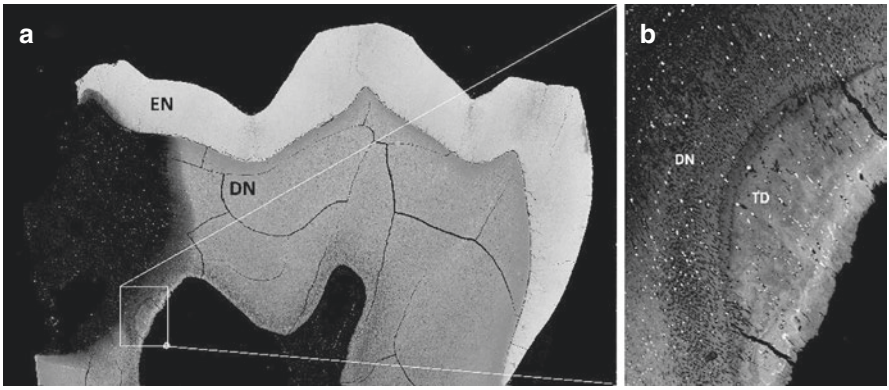

Fig. 8.3 (**a**) SEM image of a carious lesion in human tooth treated with SDF: EDS analyses confirms the silver penetration and deposition in dentin and dentinal tubules (white spots); (**b**) tertiary dentin formed after SDF treatment (*EN* Enamel; *DN* dentin; *TD* tertiary dentin). (Image copyrighted by Drs. Crystal and Rabieh, who thank Bin Hu's assistance for SEM-EDS imaging and analysis. The Zeiss Gemini 300 FE-SEM was provided courtesy of the National Institutes of Health S 10 Shared Instrumentation Program, grant number 1S10OD026989-01)

8.6 SDF as an Indirect Pulp Therapy Agent

There are only a few clinical studies done that have evaluated the clinical response of the pulp to SDF when used for indirect pulp therapy. Divyashree et al. in 2021 [36] evaluated the clinical and radiographical success of SDF 38% applied for 15 s vs. Dycal and MTA, including 25 primary molars on children aged 5–9 years in each group. The molars included in the study had caries lesions extending into 2/3 of the dentin with no spontaneous pain, and all teeth had selective caries removal and were restored with resin-modified glass ionomer cement (RMGIC). Any observed reparative dentin layer was measured radiographically and compared between groups. After 6 months, teeth treated with SDF had formed a good biological seal, further caries progression was arrested, and the SDF did not cause any adverse pulpal reaction. However, the amount of reparative dentin formed was highest in the Dycal group, followed by the MTA group with the lowest in the SDF group. Although there was no mention of clinical success and the study only followed cases for 6 months, they concluded that SDF seems to be a good IPT material as it presents with good biological seal and maintenance of pulp vitality.

In another clinical study, Patil et al. in 2021 [37] did an evaluation of 38% SDF applied for 2 min onto excavated dentin and compared it to a 1.5 mm. layer of calcium hydroxide as IPT on primary teeth on children aged 4–7 years that were followed for 6 months with 25 teeth in each group. Both groups had selective caries removal and were restored with RMGIC restorations. SDF showed 96% success rate at 6 months follow-up, whereas calcium hydroxide showed 88% success. They reported no statistically significant difference between the groups, so they conclude that SDF can be used as an effective alternative for IPT in primary molars.

In a more recent clinical trial, Shafi et al. in 2022 [38] studied the effects of diluted SDF (1:10) applied for 2 min onto excavated dentin and compared it to light-cured calcium hydroxide as IPT in 56 primary molars (28 in each group) with no signs of spontaneous pain [38]. All teeth had selective caries removal, glass ionomer cement was placed after the indirect pulp therapy agent, and they all were restored with preformed metal crowns (SSCs). They report no radiographic failures at 12 months but one clinical failure in the SDF group and two in the calcium hydroxide group, resulting in 96% success for SDF and 92.7% for calcium hydroxide with no statistical significance between the groups. Tertiary dentin deposition and discoloration of the tooth could not be evaluated as the teeth were restored with SSCs, but they conclude that 1:10 SDF diluted solution could be an alternative to calcium hydroxide for IPT in primary teeth [38].

Another recent RCT studied the clinical and radiographic effectiveness of SDF 38% with and without potassium iodide (KI) when used as indirect pulp therapy on deep carious lesions in young permanent molars restored with RMGIC (36 molars in each group) and compared it to RMGIC used as an IPT agent, followed by a resin-based composite restoration [39]. All molars had selective caries removal before the application of the pulp therapy agent. After 12 months, one failure was reported in each of the SDF and SDF + KI groups, but this showed no statistical significance in overall success between the three groups. Secondary caries was noted in only two teeth in the SDF + KI groups, but this resulted in no statistical significance between the three groups. However, they found a significant difference in the restoration color, marginal staining, and luster of the restoration, with the RMGIC group having better results than both SDF groups. They conclude that although all materials were successful at preserving pulp vitality and preventing pain, the RMGIC group showed better esthetic restorative results than the SDF groups [39].

In the USA, the original labeling of SDF and silver fluoride products was and still is as a desensitizer. Products like Riva Star (SDI Limited, Victoria, Australia) were originally marketed to reduce or eliminate dentin sensitivity on deep caries lesions. A promotional video shows it as part of the restorative treatment using a "sandwich technique" where the silver fluoride product would be applied after selective caries removal and acid etching followed by KI to reduce the staining. After rinsing thoroughly, a RMGIC was placed up to the dentin-enamel junction, covered with bonding agent, and a composite resin was placed in the surface. Since the product had a pH of 13, it was recommended to use rubber dam isolation [40]. In this technique, the first product to be placed in contact with the recently excavated dentin was silver fluoride, so in fact it would act as IPT, which would result in dentin desensitization.

8.7 The Role of SDF in Caries Management

All of the laboratory and clinical evidence to date indicate that the effect of SDF spans throughout the surface and body of the carious lesion and into the pulp chamber. Whether it is used as a desensitizer agent in IPT as part of a restorative technique with selective caries removal or by itself as a caries arrest medicament with no caries removal, it seems that the immediate formation of a hard barrier that may impede the progression of cariogenic microbes or their metabolites into dentin gives the pulp tissue time for healing, allowing formation of tertiary dentin and resulting in desensitization. All of these actions make SDF an invaluable tool for caries management. Although the staining it produces may limit its use as IPT on patients who prefer esthetic restorative treatment, its use as a caries arrest agent on patients who can't receive traditional restorative treatment is invaluable. Patients who are very young, the elderly, patients with special healthcare needs, those whose treatment has to be delayed for health or other reasons, individuals that encounter barriers for the provision of care, or those who prefer a minimally invasive approach for their dental treatment can now have the alternative of choosing a therapy that can delay or defer more complicated and expensive options. Hard-to-clean lesions with persistent plaque deposits can be selectively restored with RMGIC, and dark arrested lesions can be covered with esthetic restorative options at a later date according to the patient's situation and preferences.

Eliminating sensitivity of exposed lesions can allow for implementation of improved home care routines that in turn will help sustain the arrest of the lesions and lead to improved oral health. The evidence we have included in this chapter indicates that in order to achieve this, a reduction of the frequency of ingestion of cariogenic snacks and beverages through dietary counseling is also required. In order to evaluate and reinforce the lifestyle habits that affect the success of SDF, as well as to monitor lesions and re-apply SDF therapy as indicated, frequent re-care on these high caries-risk patients is imperative [41].

For all these reasons, we stress that the use of SDF should be part of a comprehensive caries management plan with the aim of leading the patient to sustained oral health.

8.8 Conclusions

SDF's antibacterial and remineralizing effects on treated dentin, which result in reduced bacterial load, reduced dentinal degradation, and dentinal tubules blockage, seem to allow the pulp to recover from the bacterial attack, inducing desensitization and formation of tertiary dentin. Its use as a single agent, or followed by a restoration that will further seal the dentinal tubules and protect the pulp complex, is an invaluable tool in the management of dental caries, especially when other means for treatment are not available.

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Guidance to Achieve Clinical Pulpal Diagnosis and Operative Decisions

9

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9.1 Introduction

The etiology for pulpal and periapical diseases is mainly related to caries and/or traumatic injuries. It is well established in the literature that improper diagnosis and preventive treatment can result in patients' visits to the emergency room that otherwise could be avoided [1, 2]. Reaching an accurate diagnosis is the goal of every practitioner treating any condition. The road to achieve this goal is not always straightforward. It consists of collection, assessment, and interpretation of relevant information such as (a) medical, dental, and social histories; (b) chief complaint and presence of signs and symptoms; (3) objective clinical tests in combination with clinical and radiographic examinations; (4) establishment of a tentative diagnosis by comparing clinical and subjective findings; and (5) final diagnosis when the operative approach is executed [3].

When treating children, some of the information compiled may be subjective in nature and not always directly obtained from the child but from the parent or caregiver. Some sensibility tests such as thermal and electric are of limited use in preschool children, not because of questionable accuracy but mainly due to anxiety and the potential of promoting disruptive behavior and the reliability and reproducibility of the responses obtained [4]. However, the experienced and talented clinician together with his/hers must-needed bond with the patient and the use of efficient behavior guidance techniques may allow some of these tests to be performed at an early age. A decision tree or flowchart for guidance on how to achieve treatment decisions is a desirable tool to have. Exceptions to these guidelines may include, but not limited to, patients with complex medical histories, the child's ability to cooperate, restorability of the tooth, financial considerations, and parental preferences [5].

One can only diagnose pathology when healthy and normal structures are known and familiarized by the clinician. Facial swelling and the presence of lymphadenopathy in submandibular and cervical areas are abnormal extraoral features (Fig. 9.1). Intraoral swelling, sinus tract and fistula adjacent to a tooth or teeth with history of trauma, deep carious lesion or previous existing restoration, abnormal mobility, and sensitivity to percussion when a tooth is not close to its natural exfoliation time are signs of concern (Fig. 9.2a, b) [6].

Radiographically, in primary molars, lack of lamina dura and furcation radiolucency and presence of internal and/or external resorption indicate advanced pulpal degeneration (Figs. 9.3 and 9.4). In primary canines and incisors with deep caries lesions of after traumatic injuries, widening of the periodontal ligament around the root surface and/or periapical area may indicate pathology or infection. In those situations, conservative treatment is no longer possible.

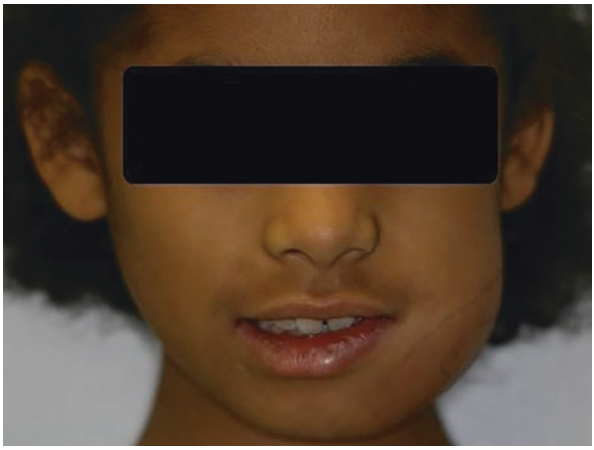


Fig. 9.1 Facial swelling as result of an odontogenic infection involving a mandibular left second primary molar. Fever and restricted mouth opening required hospital admission for IV antibiotics

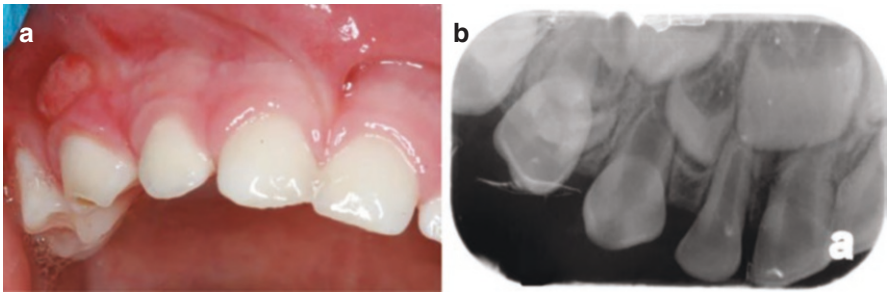


Fig. 9.2 (**a**) Apical fistula as result of incisal caries on maxillary primary canine on a 3-year-old child. (**b**) Periapical radiograph of the same tooth, showing interruption of continuation of root development as result of pulp necrosis

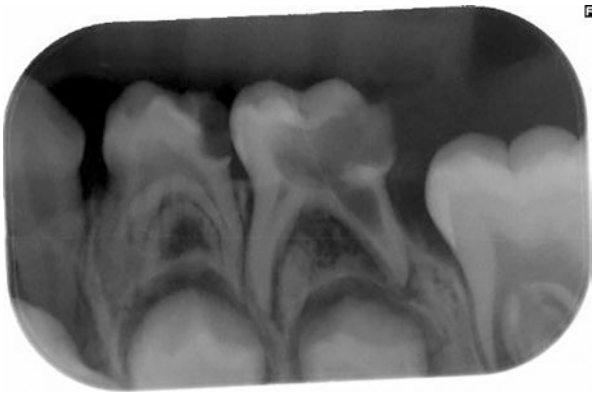


Fig. 9.3 Internal root resorption on tooth #K (75) as result of deep caries and chronic inflammation

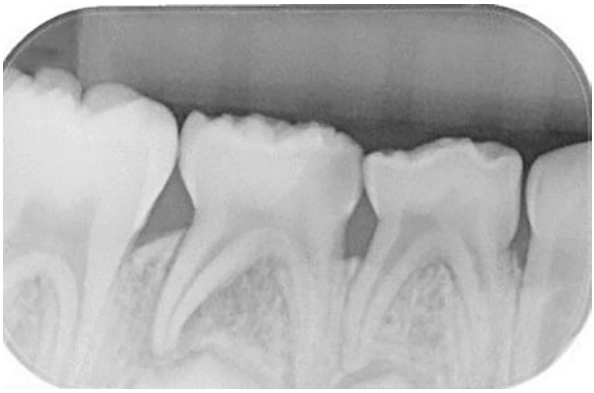


Fig. 9.4 Deep carious lesion with furcation, widening of the periodontal ligament, and periapical involvement on tooth #T (85)

9.2 Clinical Examination

During clinical examination, it is important to ask questions related to the location, duration, intensity, initiator, and inhibitor of pain. Additionally, it is very helpful to note the child's behavior and possible clues about the pain such as the holding of a specific area of the jaw and the history of provoked, nocturnal, or spontaneous pain. In the presence of diffuse or localized swelling, the palpation test will determine the extent and type of swelling (indurated or fluctuant), and body temperature is recorded (Fig. 9.1). Lymph nodes of the neck also need to be palpated to determine any possible systemic involvement. Some of the infections associated with posterior teeth, especially mandibular and maxillary molars, can be extremely dangerous and may require emergency treatment at the hospital since swelling may compromise the airway. Areas of extensive decay, traumatic injuries, and defective restorations also have to be examined.

The determination of the pulpal and periapical diagnosis is quite complex. The pulpal tissue is a connective tissue composed of nociceptive fibers. The main fibers are the myelinated A δ and unmyelinated C fibers. These nociceptive fibers play an important role during the vitality test of the pulp when the tooth is either stimulated by a thermal or an electrical current (EPT) [7, 8]. Cold and EPT do not assess pulpal vitality but the response of the nociceptor fiber to a cold and electrical stimulus, which indicates the inflammatory condition of the pulp when a chief complaint is reproduced. The reliability of the vitality test is not 100%. Peterson et al. demonstrated that 83% of the teeth with a necrotic pulp were identified as necrotic by the cold test, while 93% of the teeth with vital pulp were identified as vital by the cold test. When the electrical test was used, 72% of the teeth with necrotic pulp were identified as necrotic, while 93% of the vital teeth were identified as vital [8]. The lack of accuracy and the presence of false-positive and false-negative responses increase the challenge of determining a proper pulpal diagnosis. The lack of correlation of clinical and histological diagnosis of irreversible pulpitis could be as high as 84.4% [7, 8]. Multirooted teeth also can be partially necrotic, and due to remaining vital tissue in one of the roots and the fact that nerve fibers are the last to die, a

normal response will still be elicited when cold is applied, despite the necessity of root canal treatment due to a diseased pulp [7–9]. When treating pediatric patients, it is important to remember that due to the incomplete development of the plexus of Raschkow, until the teeth are fully occluded, the electrical test becomes more unreliable [9]. Therefore, the necessity of a good clinical history, current clinical findings, and a proper image of the tooth is of paramount importance. The lack of correlation between clinical and histological findings is well established and increases the clinician's complexity for a proper diagnosis with the vitality tests we routinely use [10, 11].

Sensibility is defined as the ability to respond to a stimulus [10–12], and hence this is an accurate and appropriate term for the typical and common clinical pulp tests such as thermal and electric tests given that they do not detect or measure blood supply to the dental pulp. The most accurate way of diagnosing pulpal disease would require histological evaluation, which is not feasible. Therefore, the clinician must rely on the diagnostic tools presented in this chapter and on the importance of reproducing the patient's chief complaint. In young permanent teeth, sensibility tests used for pulpal diagnosis are EPT, cold, and heat (when the chief complaint is pain to heat).

9.3 Diagnostic Tests

9.3.1 Electrical Pulp Test (EPT)

It is important to note that the pulpal response to the electrical current is not an indication of pulpal vitality or the health status of the pulp but the response of the sensory fibers of the pulp to an electrical stimulus. This stimulus stimulates mainly the myelinated Aδ fibers located at the odontoblastic layer of the pulp, since the unmyelinated C fibers located at the pulp proper require a higher stimulation [12, 13]. When using the EPT, the clinician should focus on a response or non-response, rather than the numerical value associated with the impulse sensation (Fig. 9.5).

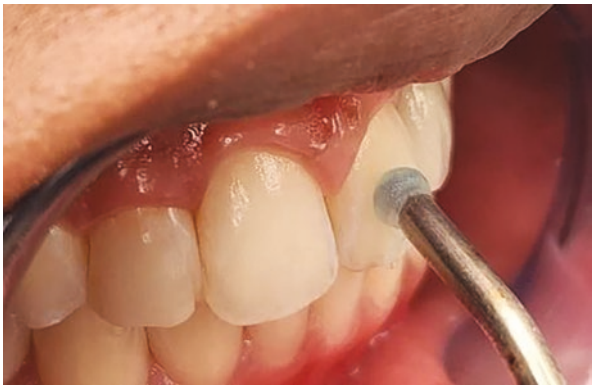


Fig. 9.5 Electric pulp test after trauma on a maxillary permanent incisor

9.3.2 Cold Test

The thermal test is one of the most used sensibility tests to determine the vitality of the pulp. In the past, different tests were used for cold, such as ice tubes, CO_2 snow, and a refrigerant spray (Endo-ice). Their mechanism of action occurs by initiating fluid movement at the odontoblastic layer of the pulp, resulting in the generation of action potentials in the nerve ending [14]. The temperature obtained with the CO_2 snow is −78.1 °C; with a ball of cotton pellet sprayed with the refrigerant, it is approximately −50.1 °C. When testing with cold or any thermal test, it is important to test a similar tooth that is not the offended one and appears normal to obtain a baseline test for comparisons. This will also decrease the child's anxiety. With the advances of new research, it is established that Endo-ice even in the presence of crowns is a very viable test, since it causes a reaction to the stimuli quicker than the one caused by CO_2 snow despite the lower temperature. When the cold test is applied on the tooth, a normal response is considered when the sensation is felt by the thermal application but disappears after the removal of the stimuli without inducing a painful or lingering response. An unusual response is obtained when the application of the stimulus triggers moderate-to-severe pain due to an irreversible degree of inflammation, or it does not elicit any sensation, which could indicate necrosis or calcification of the pulp (Fig. 9.6a, b).

Cold and EPT can be successfully performed in children at the early mixed dentition stage and serve as an indicator of the status of the pulp. Clinicians need to take into consideration the limitations of this type of tests, especially in pre-cooperative or patients with special needs [15–17].

9.3.3 Heat Test

This test is only indicated when a patient's chief complaint is pain on heat. One of the best ways to test heat is by isolating the arch with a split dam isolation and testing each tooth with a cotton ball of hot water. If the chief complaint is reproduced, the clinician can then diagnose the offending tooth.

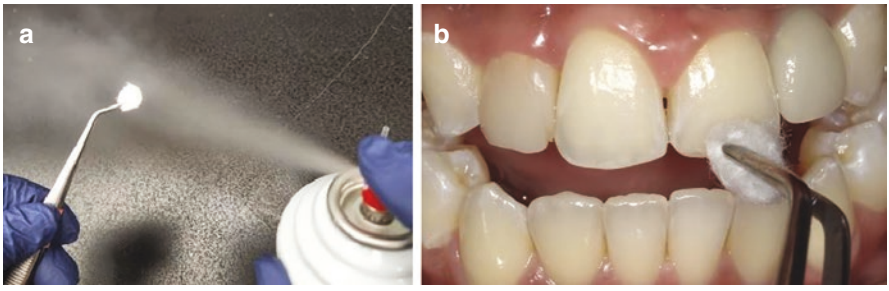


Fig. 9.6 (**a**) The refrigerant spray (Endo-ice) placed on a ball of cotton pellet instead of a cotton tip applicator for better transfer of cold; (**b**) the sprayed cotton pellet applied to the midfacial area of the tooth or crown

9.3.4 Laser Doppler Flowmetry (LDF)

Laser Doppler measures the blood flow by the dissemination of an infrared light through the pulpal tissue and the difference in frequencies when contacting red blood cells. This average frequency shift measures the velocity at which the red blood cells are moving [18, 19]. Many studies have demonstrated the use of LDF for pulpal vitality, especially following traumatic injuries. However, its use in clinical settings is not completely established due to the high cost, differences on pulp chambers due to calcifications, "noise" created by the backscattered light in contact with tissue, and the inability to create a baseline to compare normal to diseased.

9.3.5 Pulse Oximetry

This test assesses vascular integrity by measuring the oxygenation of blood. However, the validity of its use in clinical practice is still controversial [20, 21].

9.3.6 Periapical Tests (Percussion)

This test evaluates the status of the periodontium surrounding the tooth. It is best performed by tapping the handle of the clinical mirror along the long access of the tooth at the occlusal or incisal surface of the tooth and horizontally on a 90-degree angle with the crown (Fig. 9.7a, b).

In young children, the use of the tip of the finger to test percussion sensitivity is a well-accepted method. Clinicians must be aware of potential false-positive response to percussion caused by food impaction when large proximal lesions are present, which may result in inflammation of the papilla instead of pulpal in nature [22].

9.3.7 Probing

Periodontal probing is important to assess any possible periodontal involvement and potential vertical root fractures (Fig. 9.8).

9.3.8 Periapical Image

A proper periapical image is of paramount importance for the pulpal and periapical diagnosis and overall treatment planning in endodontics. In addition to periapical images, a limited focal view CBCT has been instrumental for earlier detection of resorption in traumatized teeth (Fig. 9.9a, b). Additionally, when taking periapical images, according to a classical study from Brynolf, an accurate diagnosis was

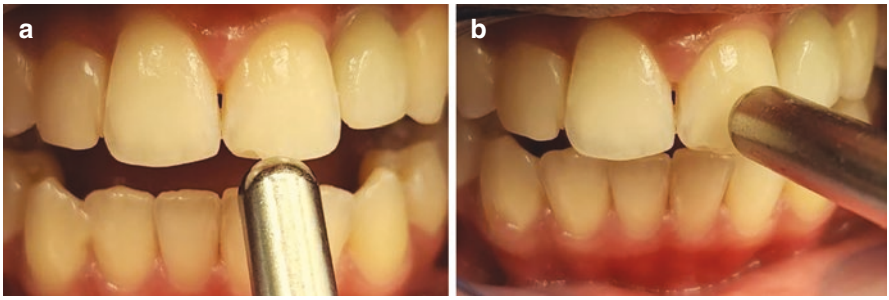


Fig. 9.7 (**a**) Percussion test on incisal edge and (**b**) percussion test on the facial surface of the tooth

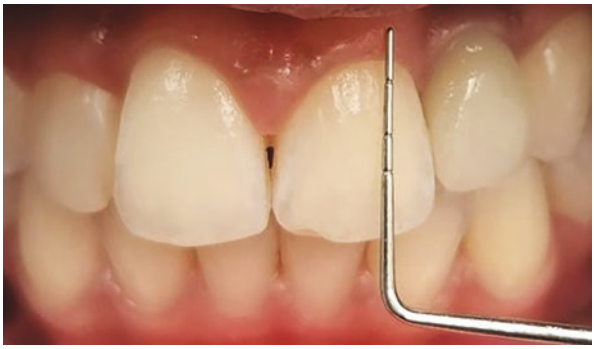


Fig. 9.8 Periodontal probing

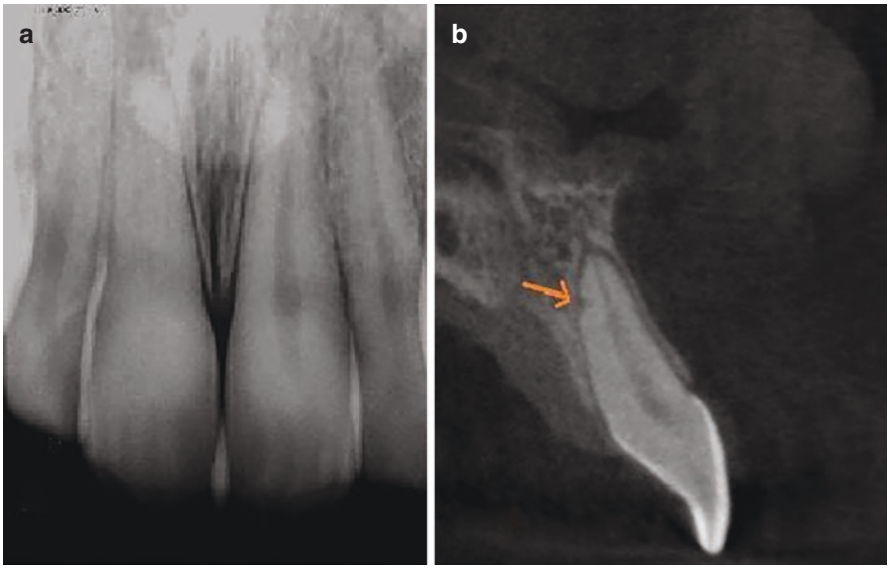


Fig. 9.9 (**a**) Periapical image of teeth #s 8 and 9. CC: tooth hurts after I hit my mouth on the basketball arch. (**b**) Early signs of inflammatory root resorption detected by the limited view CBCT. Vitality test was giving a normal response to Endo-ice and EPT. RCT was initiated, and symptoms went away

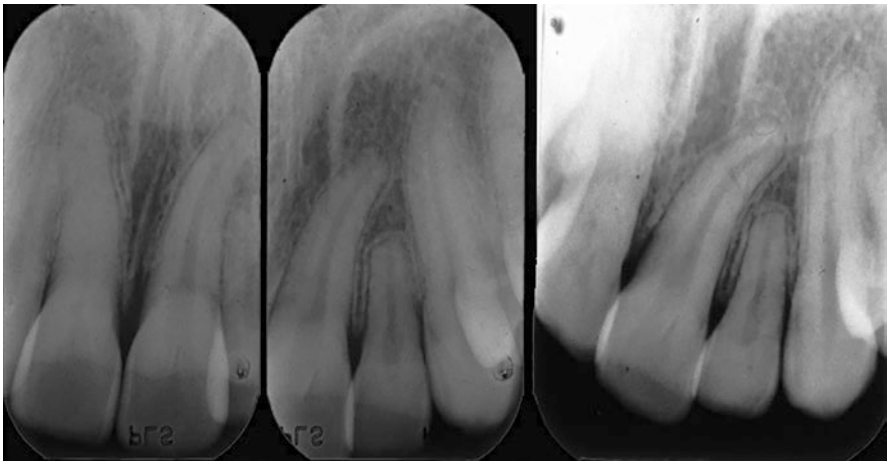


Fig. 9.10 The importance of angled radiographs for better diagnosis. The horizontal root fracture would not be detected if only one angle radiograph was taken

obtained with 90% accuracy when three radiographs were taken in different angles as compared to 74% of accuracy when one straight angle is obtained (Fig. 9.10) [23].

9.3.8.1 Focal View CBCT

The American Association of Endodontists and the American Academy of Oral and Maxillofacial Radiology in 2015 published a revised joint position statement on the use of CBCT in endodontics [24]. Among several indications for its use, both associations advocate the use of CBCT in traumatic injuries and as a tool to assist on complex cases of diagnosis (Fig. 9.9b).

9.4 Depth of Caries and Presence of Symptoms

It is important to remember that when caries is the main etiology, the clinician needs to thoughtfully diagnose the pulpal and periapical tissues to determine the treatment that can provide the best long-term outcome to the patient. If the carious tissue is not properly removed and restoration not properly sealed, especially in patients with high caries risk, bacterial by-products will continue to move through the dentinal tubules inducing more inflammation and further pulpal necrosis [7, 25, 26]. To further decrease the chance of a good outcome, the pulp has a restricted healing potential. This is caused by the lack of collateral supply, microcirculation, and the rigid structure, by which the pulp is surrounded by.

Since the histopathologic status of the pulp is currently impossible to be obtained, determination of pulp vitality in primary teeth with deep carious lesions or after trauma is more of an art than science. Coll et al., for example, suggested interim therapeutic restorations for deep carious lesions as a practical tool for determination if a conservative pulp therapy approach is possible [27]. Kassa et al. [28]

demonstrated that in occlusal and proximal lesions less than 50% deep into dentin, pulp inflammation should be minimal to none. However, when positive history of pain exists and the depth of caries is more than 2/3 into dentin and remaining dentin thickness equal to or less than 1.0 mm, presence of inflammation was a common histological finding on both coronal and radicular portions of the pulp in affected second primary molars [29]. Selection of a conservative approach, such as selective caries removal, may be contraindicated in these situations.

9.5 Bleeding and Pulpal Status

According to Aminabadi et al., accidental pulp exposures in primary molars resulted in much lighter bleeding color than when caries exposure occurred and pulpotomy was performed [30]. Darker bleeding color in primary molars was considered an indication for a more aggressive treatment approach such as pulpectomy in some studies (Fig. 9.11) [30, 31].

The ability to obtain hemostasis at the canal orifices has been a clinical indication for a potential health status of the radicular pulp [3]. However, a recent study demonstrated that the achievement of hemostasis did not provide accurate assessment of the inflammatory status of the pulp at the canal orifices and should not be used as criterion for pulpotomy [32].

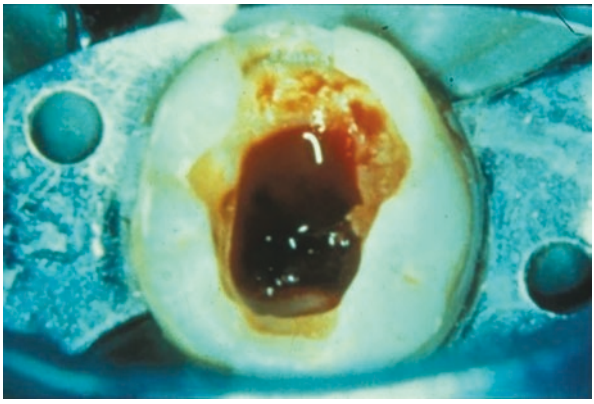


Fig. 9.11 Dark bleeding in a primary molar with a history of nocturnal and spontaneous pain. Pulpectomy or extraction may be indicated

9.6 Pulpal Diagnosis Terminology

The pulpal diagnosis can be normal, reversible, symptomatic irreversible pulpitis, necrotic, and previously treated. The tables below explain the clinical diagnostic terminology (Table 9.1) and periapical diagnostic terminology (Table 9.2) of the pulpal disease obtained from the American Association of Endodontics (AAE) Consensus Conference Recommended Diagnostic Terminology [33].

Table 9.1 The clinical diagnostic terminology of pulpal disease obtained from the American Association of Endodontics (AAE) Consensus Conference Recommended Diagnostic Terminology (2009)

Normal	The pulp is symptom-free and responds normally to pulp testing. No history of pain or sensitivity
Reversible	Patients usually complain about *hypersensitivity* to cold and/or sweets that goes away when the stimulus is removed. The subjective and objective findings demonstrate that the inflammation should subside and pulpal tissue reverse to normal when the etiology is removed
Symptomatic irreversible pulpitis	Patient presents with pain or history of unprovoked pain. When the cold stimulus is applied, the pain is severe or lingers. The main etiologies are deep caries, extensive restorations, or fractures exposing the pulpal tissues. The pulp cannot heal, and the inflammation cannot be reversed to normal. Root canal treatment is indicated
Asymptomatic irreversible pulpitis	Vital inflamed pulp is incapable of healing, and root canal treatment is indicated. These cases have *no clinical symptoms* and *usually respond normally to thermal testing* but may have had trauma or deep caries that would likely result in exposure following removal (Fig. 9.12)
Necrotic	A clinical diagnosis indicating death of the pulp tissue. The pulp is usually non-responsive to sensitivity testing
Previously treated	Indicates the diagnosis of a tooth that had been endodontically treated and the canals obturated

Table 9.2 The clinical diagnostic terminology of the pulpal and periapical disease obtained from the American Association of Endodontics (AAE) Consensus Conference Recommended Diagnostic Terminology (2009)

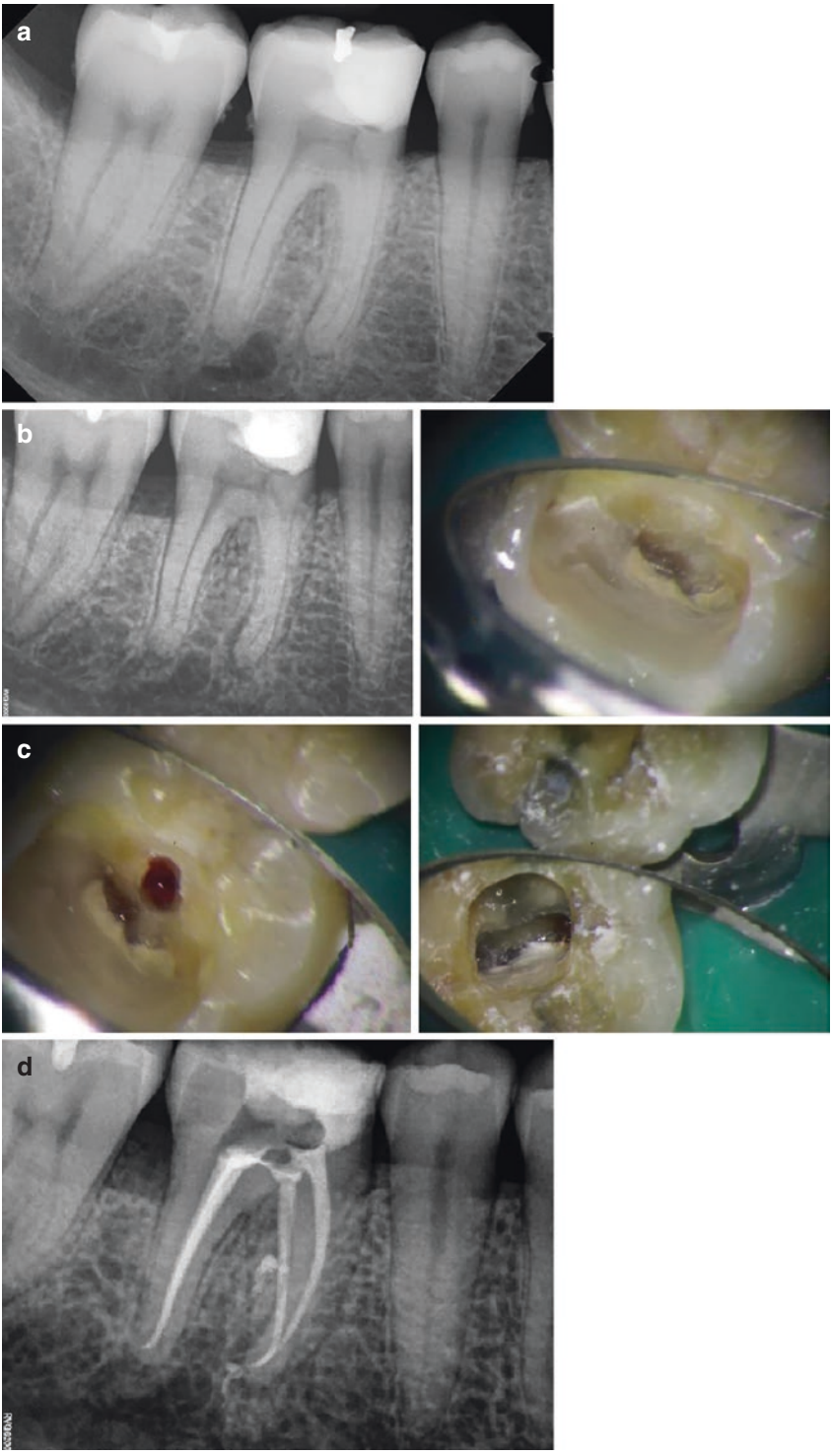
Normal	The periapical tissue surrounding the root of the tooth appears normal. The lamina dura is intact. The percussion and palpation tests are normal, not eliciting any pain and or discomfort
Symptomatic apical periodontitis	The periapical tissue is inflamed. Pain to percussion and/or palpation. CC might be associated with pain from biting. Periapical radiolucency might or might not be present
Asymptomatic apical periodontitis	Patient presents with no pain to percussion and/or palpation. Inflammatory reaction has caused the presence of a periapical radiolucency
Chronic apical abscess	Characterized by an inflammatory reaction to pulpal infection and necrosis with little or no discomfort and the presence of a sinus tract
Acute apical abscess	A clinical diagnosis indicating death of the pulp tissue. The pulp is usually non-responsive to sensitivity testing. Characterized by rapid onset, spontaneous pain, and pain to percussion and palpation. Presence of swelling and pus
Condensing osteitis	Characterized by diffuse radiopaque lesion representing a localized bone reaction to a low-grade inflammatory stimulus, usually seen at the apex of the tooth

9.7 Conclusion

As previously stated, one of the main challenges in dentistry is the ability to properly diagnose. Despite the advances in technology, at this point, we are still relying on cold and an electrical current as the main tools for the diagnosis of the pulpal tissue. The advances in biological markers and in image modality with artificial intelligence will hopefully bring another tool for us practitioners. In the meantime, we clinicians need to understand the subjectivity of the vitality tests and remember that the bacterial by-products will cause an inflammatory and chronic infection that could lead to pulpal necrosis, despite a normal response to vitality tests.

The case below illustrates a tooth that was diagnosed as normal pulp despite the large amount of caries in proximity to the pulp chamber and the previous history of pain (Fig. 9.12a–d).

Fig. 9.12 (**a**) 15-year-old male patient with large occlusal caries and high caries risk due to poor hygiene and diet. Due to a normal response to the vitality test, the tooth was diagnosed as normal pulp rather than asymptomatic irreversible pulpitis. An indirect pulp capping was performed. Four weeks later, the patient had severe percussion pain and a dull pain on the lower arch. (**b**) Presence of a periapical radiolucency, soft carious tissue encountered under the permanent filling near the Dycal liner. Vitality tests were performed and tooth diagnosed as necrotic with symptomatic apical periodontitis. (**c**) As noted, the tissue looked unhealthy, and the other two canals appeared necrotic. (**d**) *Root canal treatment was performed and symptoms subsided. Patient received a full-coverage crown*


a
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Management of Deep Dentin Carious Lesions: A Contemporary Approach for Primary and Young Permanent Teeth

10

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10.1 Introduction

Caries prevalence is still high worldwide, with the disease burden affecting all age groups [1]. When biofilm control and preventive measures fail, a carious lesion is expected to develop. Following its natural developmental history, the lesion will advance through the enamel and reach the dentin, leading to pulp infection and necrosis.

If appropriate control measures are implemented, such as biofilm control, adoption of a healthy diet, and rational use of fluoride, the lesion can be controlled, and remineralization of the dental tissue may occur. As discussed in Chap. 6, this is true for non-cavitated carious lesions and even for cavitated ones, as long as the patient is able to clean the lesion properly on a regular basis. However, in the presence of a cavity with no possibility of biofilm control inside it, the lesion is likely to progress, and the appropriate treatment is the placement of a restoration. Early management of deep carious lesions can arrest demineralization and reduce the need for pulp therapies. This chapter will guide the reader in the management of deep dentin carious lesions in the aim of improving patients' health.

10.2 Dental Caries Lesion Development and Pulp Reactions

Dental caries results from an interaction between the microbial biofilm and the mineralized dental tissues. Imbalance between the physiological processes of demineralization and remineralization with predominance of demineralization events will cause mineral loss from dental tissues with consequent formation of the carious lesion.

As thoroughly described in Chap. 6, the first stage of carious lesion development involves erosion and porosity of the enamel surface. A subsurface lesion is formed just below the enamel, and if no treatment is provided and the disease continues, increased porosity of the outer surface is established, with an increased subsurface demineralization. This can lead to the formation of a cavity, which first reaches the enamel and then the dentin on the coronal part of the tooth (or the cement and the dentin in the tooth root) and, finally, leads to the total destruction of the tooth.

Very early in the carious process, due to the porosity of the enamel, stimuli from the oral cavity pass through this tissue into the dentin. Dentin and pulp can be considered one entity, as odontoblast processes pass through the dentinal tubules. As bacterial acid, plaque metabolic sub-products, and bacteria wall components such as liposaccharides reach the dentin-pulp organ, different reactions can occur [2, 3]. The first alteration is the hypermineralization of the dentin just below the enamel lesion even before the demineralization reaches the dentin. First, a secretion of highly mineralized peritubular dentin is observed, which will reduce the diameter of the tubule. Intratubular deposits of mineral also take place [4]. Enamel demineralization takes place in the affected hypermineralized dentin. The first indications of cellular reactions are noted in active lesions involving about 1/4 of the enamel layer, but without discernible alterations in dentin mineralization [5].

Bacterial products diffuse through the dentinal tubules and may induce inflammatory response from the pulp even before it is exposed. The inflammatory process initiates already in the presence of non-cavitated enamel lesion [6] and intensifies as the demineralization reaches the dentin. During dentin demineralization, a series of products that have been trapped in the dentin during its mineralization are released. The pulp responds to the microbial product invasion, through the permeable tissue, liberating or activating mediators form polymorphonuclear and mononuclear leukocytes. Dentin-pulp complex permeability is likely to be reduced in carious teeth due to tubular sclerosis subjacent to the carious dentin.

Growth factors released during dentin demineralization could be related to tertiary dentin formation, which seems to occur when the demineralization reaches the dentin. Tertiary dentin formation is another form of pulp protection organized by pulp cells in response to caries' advance. The structure of tertiary dentin depends on lesion activity, i.e., on the severity of the irritating stimuli, and can be divided into two types: reactionary dentin, formed by the odontoblasts present in slow progression lesions (in mild irritation), and reparative dentin, formed by the odontoblast-like cells that differentiate from pulp stem/progenitor cells after the death of the odontoblasts (in severe irritation) [7]. The faster the progression of the lesion, the more irregular the structure of the newly formed tertiary dentin is, even with cellular inclusion. At this stage, lesion progression can be controlled, and the inflammation can subside, if the biofilm is regularly removed or the cavity is isolated from the oral environment by a restoration. However, when bacteria reach the tertiary dentin, the number of inflammatory cells is abundant. At this stage, usually severe pulp inflammation occurs, with decreased healing chances. Areas of necrosis in the pulp are not seen until the microorganisms reach the pulp [8]. The management of deep carious lesion is linked to the inflammatory pattern of the pulp.

10.3 Different Stages of Dental Caries Lesions, Dental Tissue Bacterial Invasion, and Lesion Control

For many decades, the decision between a conservative treatment and an invasive treatment for dental caries lesions was related to the presence of microorganisms inside the dental tissue. Control of non-cavitated lesions without the necessity of restorations is well established since the 1980s [9], and it was also supported by the traditional understanding that non-cavitated lesions harbored no bacteria and therefore could be controlled with no tissue removal. On the other hand, once a cavity was formed and microorganism was present inside the dental tissue, this contaminated tissue had to be removed and a restoration be placed to control lesion progression. Notwithstanding, studies showed the presence of microorganisms even in non-cavitated lesions, in both enamel [10] and dentinal tubules [11], which does not prevent lesion arrestment. In addition, despite the great amount of microorganisms invading the dentin tissue once a cavity is formed, Anderson, already in 1938, showed that cavitated lesions of molars can be arrested once the biofilm is removed [12]. Another body of evidence that dentin caries can be controlled with no invasive

therapy is the root lesions. With the increased tooth retention currently observed in the adult and elderly population, a large number of arrested cavitated root lesions have been observed. In addition to this evidence derived from observational data, intervention studies also showed the possibility of arresting root carious lesions by adopting noninvasive therapies [13]. All this evidence shows that (1) the presence of microorganism within the dental tissue does not prevent lesion control and (2) carious lesions can be controlled once the external biofilm is regularly removed, independent of the microorganism invasion of the dental tissues.

Despite this knowledge, the elimination of carious dentin was considered essential to control the carious process for many decades. Traditionally, it was recommended to remove "all the carious tissue" prior to the placement of a restoration, until reaching dentin with clinical characteristics similar to those of healthy tissue in terms of hardness and staining. As early as 1908, when devising a logical sequence of procedures for the cavity preparation, Black [14] suggested that the cavity would be adequately clean and ready to receive the restorative material when it presented sufficient probing resistance to promote the "dentin scream," in addition to color similar to sound dentin.

Later studies from the 1950s and 1960s have already shown that the removal of carious tissue based on hardness criteria does not eliminate microbial contamination and that there is no relationship between tissue hardness and its level of contamination. Macgregor, Marsland, and Batty [15], when evaluating bacterial growth after total removal of softened dentin, showed that 51% of the evaluated teeth presented viable bacterial colonies. Whitehead, Macgregor, and Marsland [16], using the same methodology, demonstrated that the dentin, although hard, presented microbial growth in 75.5% of the primary teeth and 49.5% of the permanent teeth. Similarly, Shovelton [17] observed histologically that 36% of teeth with hard dentin had microbial contamination, while 39% of cases with leathery dentin and 28% of teeth with soft dentin were free of microorganisms. Using a molecular biology technique called in situ *hybridization*, Banerjee et al. [18] quantified the total population of viable bacteria in different dentin layers at different depths (superficial, medium, and advanced – the latter corresponding to the hard dentin usually kept after cavity preparation). Many microorganisms were found at all depths, including the dentin layer considered healthy. This reinforces the absence of association between the clinical aspect and level of contamination.

These results allow us to infer that the maintenance of bacteria under the restoration, which routinely occurs in dental practice, does not cause clinical failure. This knowledge gave rise to conservative treatment strategies for carious lesions of different depths, freeing the dentist from the obligation to remove all the carious dentin as a fundamental premise for treatment success.

Sealing carious lesion forms a physical barrier and cuts off the nutrients from the oral cavity to the cariogenic microorganisms. Studies on sealing carious tissue under sealants or restorations have shown reduction or complete elimination of the population of viable microorganisms [19–26], thus controlling caries progression. A clinical study compared the microbiological infection (in culture) immediately after conventional carious dentin removal and a conservative caries removal with

sealing of carious dentin for six months. Significantly less anaerobic bacteria, aerobic bacteria, and *Streptococcus mutans* growth was observed after sealing carious dentin than after traditional dentin caries removal [27].

Based on the abovementioned studies, it can be concluded that:

- Microorganisms invade the dental tissue already in non-cavitated lesions.
- Microorganisms within the dental tissue (either enamel or dentin) do not preclude lesion arrestment, as long as it is possible to control the external biofilm.
- When it is not possible to control lesion progression through biofilm control, sealing carious lesions or placing a restoration is necessary, depending on lesion depth.
- There is no relationship between dentin hardness and level of bacterial contamination.
- The traditional methods of carious dentin removal usually leave microorganisms within the hard dental tissue left at the bottom of the cavity preparation before restoration.
- It is not necessary to remove all carious dentin before the restoration is placed because, over time, sealing of carious dentin results in lower levels of infection than traditional dentin caries removal.

10.4 Treatment Options for Deep Dentin Carious Lesions

The traditional approach for the management of deep carious lesions was based on complete (or nonselective) caries removal, which results in a higher risk of pulp exposure, as widely demonstrated in the literature [20, 28–30]. Regardless of the dentition, whether primary or permanent, regardless of the study design, randomized trials or not, studies are unanimous in demonstrating that this strategy results in a higher risk of pulp exposure in comparison with less invasive techniques. Indeed, recent consensus reports have stated that complete or nonselective caries removal is no longer recommended; it is considered overtreatment according to current concepts for caries removal [31, 32]. The recent systematic review with meta-analysis by Schwendicke et al. [33] concluded that less failures were observed for conservative techniques based on selective caries removal or no caries removal in comparison with nonselective caries removal, for both primary and permanent dentition.

In an attempt to avoid pulp exposure, different treatment strategies have been proposed over the last decades for the clinical management of deep carious lesions. Several investigations in the last century have already demonstrated that decayed dentin could be retained so that pulpal exposure could be avoided during cavity preparation [34, 35]. The treatment, called indirect pulp capping (IPC), performed mainly on primary teeth, is based on excavating decayed dentin as much as possible without pulp exposure. In this technique, only a thin layer of carious dentin is left over the pulp. Microbiological studies showed that, although the deep layer of residual carious dentin left during IPC is almost always contaminated, this layer was either rendered sterile or the number of microorganisms was greatly reduced after

sealing [36]. More recently, however, the European Organization of Endodontology defined IPC as a therapy that leaves neither soft nor firm carious dentin behind [37].

The most conventional option for the conservative management of deep carious lesions is the stepwise excavation (SW) technique, currently seen as selective caries removal to firm dentin (SCR-FD) in two visits. In this approach, only the necrotic layer of carious dentin is removed from the pulpal/axial cavity walls at the first visit, during the acute phase of caries progression (this stage is currently called selective caries removal to soft dentin [SCR-SD]), followed by cavity lining with calcium hydroxide cement, glass ionomer cement, or hydraulic calcium silicate cement and temporary restoration [37]. In the second visit, SCR-FD is performed, and a restoration of long-lasting material is placed. The aim of the first stage is to change the cariogenic environment, replacing an active carious environment, clinically identified by a soft, discolored, and wet tissue, by an arrested carious environment, characterized by a darker, harder, and drier appearance [3, 37]. From a clinical/practical perspective, the reasoning behind this technique is that after a given time, the dentist will be able to reach firm dentin with no/lower risk of pulp exposure. Studies comparing SW with nonselective caries removal have shown that the two-step procedure significantly reduces the risk of pulp exposure [20, 28–30, 37]. The most robust evidence on this topic was generated by a 5-year randomized clinical trial that showed 60.2% of success for SW compared with 46.3% success for nonselective caries removal to hard dentin ($P = 0.03$) when pulp exposures per se were included as failures. Non-exposed pulp of teeth submitted to conventional dentin caries removal was 50% (95% CI = 1.01 to 2.2, $P = 0.04$) more likely to fail than the SW-treated teeth. In general, SW was superior to nonselective caries removal, with less pulpal exposure, less pain and more teeth with vital pulps in the SW group [38].

The clinical changes that occur in sealed carious dentin after the first session of SW led to questioning the need for reopening the cavity for final excavation and gave rise to a series of studies on this topic. Several studies using different methodologies have assessed the effect of sealing carious dentin, in both shallow and deep lesions. These studies may be categorized according to the outcome under investigation into:

- Clinical evidence: replacement of softened and yellowish tissue by harder and darker dentin after cavity sealing, both in shallow [39–41] and deep [20, 24, 26, 42–45] carious lesions (Fig. 10.1)
- Laboratorial evidence: increased hardness perceived in tactile inspection of sealed carious dentin confirmed by microhardness analyses performed on exfoliated primary teeth [46, 47]
- Biochemical evidence: increased mineral content after sealing carious dentin, with higher levels of calcium [43] and phosphorus [48]
- Radiographic evidence: increased radiopacity in the radiolucent zone beneath the restoration [24, 49] (Fig. 10.2)
- Structural evidence: structural reorganization of sealed carious dentin, with total or partial obliteration of dentinal tubules observed by scanning electron microscopy analyses [43, 50] (Fig. 10.3)

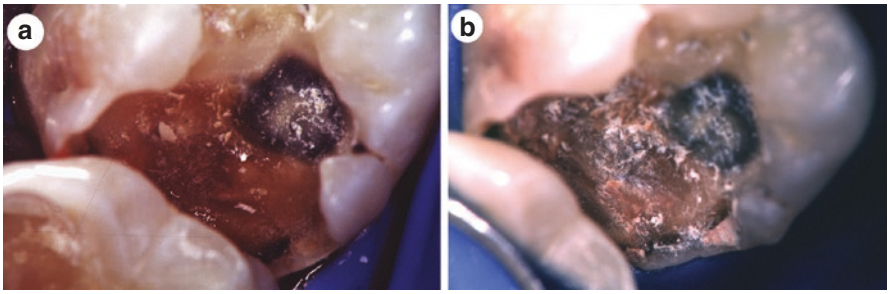

Fig. 10.1 Carious lesion immediately after SCR-SD, with a softened and yellowish tissue (**a**); clinical aspect after 6 months of cavity sealing, with a harder and darker tissue (**b**)

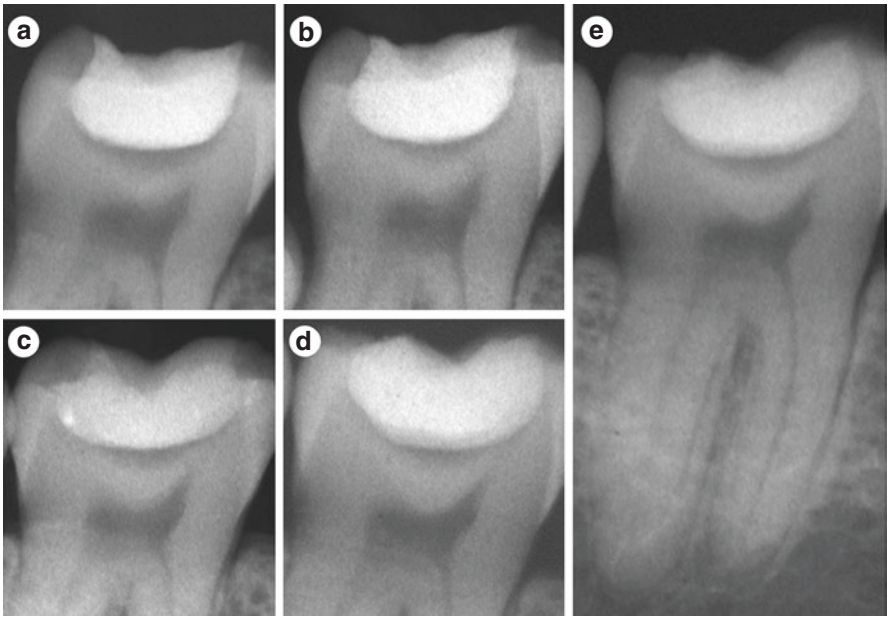

Fig. 10.2 Tooth treated with SCR-SD. Bitewing radiographs taken at baseline (**a**), after 6–7 months (**b**), 3 years (**c**), and 10 years (**d**). The 10-year follow-up periapical radiograph shows a normal periapical area (**e**). Increased radiopacity of the carious dentin left beneath the restoration can be observed [49]

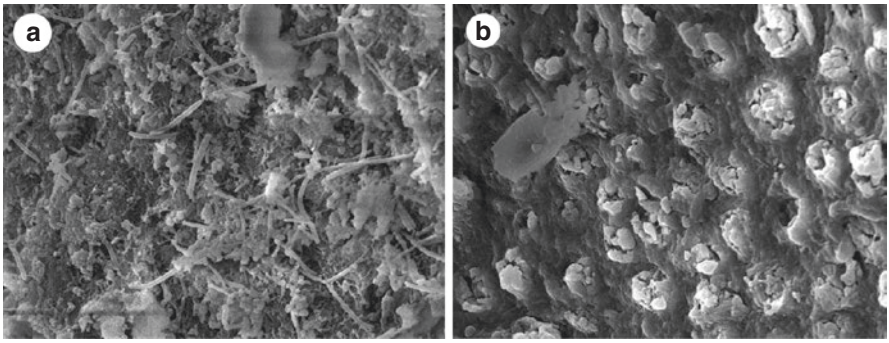

Fig. 10.3 Scanning electron microscopy photomicrographs (×3000) of dentin samples. Disorganized dentin structure with exposure of inter-tubular dentin collagen fiber and bacterial infection after SCR-SD (a); more organized dentin with total or partial obliteration of dentinal tubules and a reduction in bacterial infection after a 3-month sealing period with wax (**b**) [44]

- Microbiological evidence (quantitative assessment): reduction in the number of viable bacteria when the caries lesion was isolated from the external environment, either through the use of sealants or restorations [20–26, 36, 39–44, 50–52], achieving lower levels of infection than traditional dentin caries removal [27]
- Microbiological evidence (qualitative assessment): changes in the composition of the microflora, with less complex and less cariogenic microbiota after sealing [52, 53]

In addition to this body of evidence supporting the SCR-SD as a one-visit technique, some disadvantages of the two-visit procedure (associated with the need for a second visit to complete the treatment) also became evident:

- Additional cost [54–57], time, and discomfort to the patient.
- Possibility of pulp exposure during the final excavation, around 15–17.5% [28–30].
- Risk of patient absenteeism in the second visit, leading to fracture or loss of temporary filling and, consequently, lesion progression [58–60].

Based on all this evidence, it became clear that once carious dentin is isolated from the nutrient supply, deep carious lesions can be managed by SCR-SD. Considering

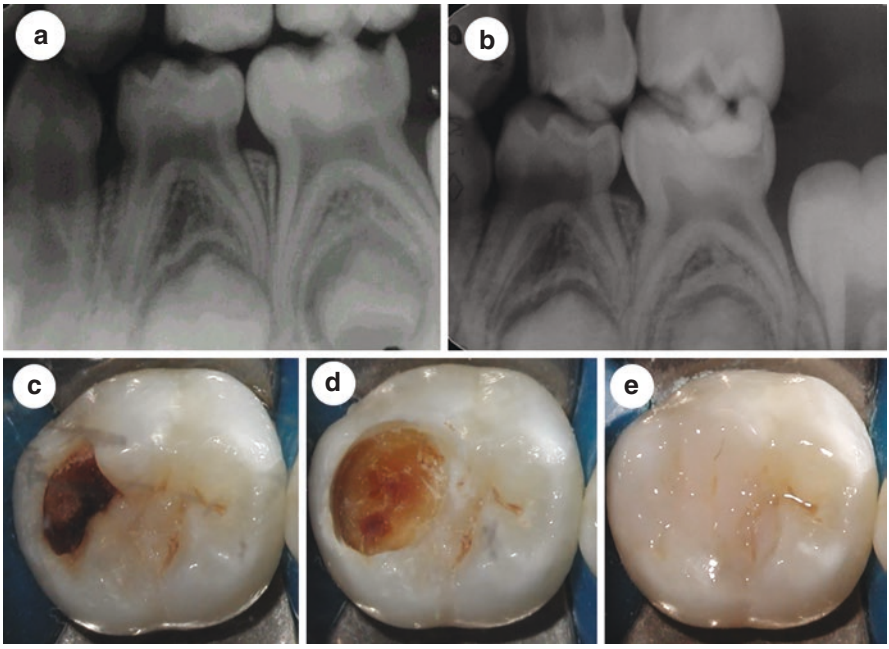

Fig. 10.4 Clinical and radiographic images of SCR-SD in a primary tooth. Periapical radiograph of tooth 75 with radiolucent image extending to the inner half of dentin (**a**). Radiographic aspect after cavity restoration (**b**). Clinically, the lesion presents as a large cavitated lesion (**c**). Clinical aspects of the cavity after nonselective removal of carious tissue from the surrounding walls and SCR-SD at the pulpal wall (**d**). Composite resin restoration (**e**)

that an effective isolation from the nutrient supply is only achieved by adequate marginal sealing of the cavity, it is worth mentioning that the peripheral/lateral walls of the cavity must be excavated to hard dentin. Therefore, SCR-SD should be restricted to the pulpal/axial walls of the cavity (Figs. 10.4 and 10.5).

Before the publication of recent consensus reports [31, 32] this technique was also known as partial, incomplete, minimally invasive, or ultraconservative caries removal. For standardization purposes, the current terminology used in the literature for caries removal techniques was adopted in the present chapter.

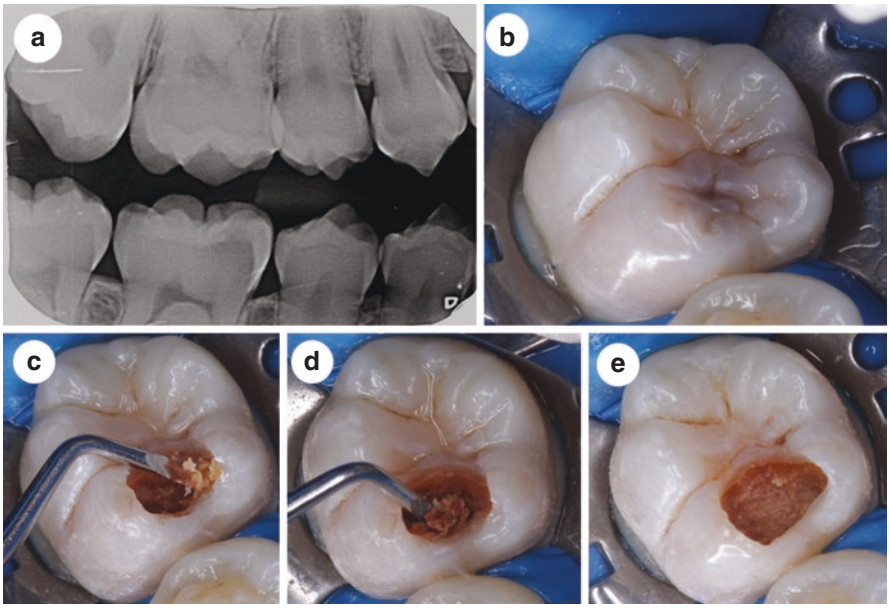

Fig. 10.5 Clinical and radiographic images of SCR-SD in a permanent tooth. Bitewing radiograph of tooth 46 with radiolucent image extending to the inner half of the dentin (**a**). Clinically, the lesion appeared as an underlying dentin shadow on the mesial portion of the tooth (**b**). Complete removal of carious tissue from the surrounding walls (**c**) and SCR-SD at the pulp wall using a hand excavator (**d**). Final appearance of the cavity after SCR-SD (**e**). Images are courtesy of MSc Rafael Schultz de Azambuja

10.5 Clinical Evidence for Primary Teeth

Clinical studies assessing the effectiveness of SCR-SD are usually focused on two different outcomes: maintenance of pulp vitality and restoration longevity. Regarding the maintenance of pulp vitality, similar success rates were found for SCR-SD (92%) and nonselective caries removal (96%) [61] after 24 months of monitoring. This study also showed that the operative time was significantly higher for nonselective excavation, which is an important aspect to be considered – mainly during the treatment of children. This study was recently corroborated by a multicenter randomized clinical trial that also compared the SCR-SD technique with nonselective caries removal and found high (≥96.5%) success rates for both strategies, with no difference between them [62]. In a series of studies performed at the Federal University of Rio Grande do Sul, the success rate of SCR-SD in primary molars ranged from 79% to 96% after follow-up periods from 2 to 5 years [63–68].

Another possible concern related to the SCR-SD technique that has motivated some studies in this research field is the risk of reduced restoration longevity due to the maintenance of decayed tissue beneath the restoration. A systematic review with meta-analysis on this topic that included four studies found that SCR-SD increased the risk of experiencing restoration failure [69]. The risk of bias of the studies

included was classified as high, and the quality of evidence was low, which led the authors to conclude that the evidence level was insufficient for definitive conclusions. In fact, taking a closer look at the four studies included in this systematic review, two studies assessing glass ionomer restorations have not found difference between the study groups [70, 71], while another one detected no failure over the study period in any of the comparison groups [72]. Therefore, there is only one study in the literature showing lower success rates for resin restorations after SCR-SD than after nonselective caries removal in deep carious lesions of primary molars [61, 73]. After 24 months of follow-up, the authors found 66% of success rates for restoration in primary molars after SCR-SD and 86% after nonselective caries removal ($p = 0.03$) [61], with these rates decreasing to 57% and 81%, respectively, after 36 months of monitoring ($p = 0.004$) [73].

Another recent randomized clinical trial compared SCR-SD and SW for the management of deep carious lesions in primary molars [57, 74]. Similar success rates were observed after 12 [74] and 24 months [57] regarding the primary outcome of the study [57]. The authors concluded that the significantly higher costs for performing the two-step procedure instead of the one-step treatment may not be justified. It is important to mention that the International Caries Consensus Collaboration organized by the European Organization for Caries Research has not recommended SW for the management of deep carious lesions in primary teeth [31].

10.6 Clinical Evidence for Permanent Teeth

Studies including permanent teeth are less abundant in the literature. The pioneering study coordinated by Maltz et al. followed patients with deep carious lesions in permanent posterior teeth who underwent SCR-SD and resin restoration for 6–7 months [24], 14–18 months [75], 3 years [76], and 10 years [49, 77]. After 5 and 10 years of monitoring, success rates were 82% and 63%, respectively, when all reasons for failure were combined (restoration fractures and pulp necrosis). When the failures caused by fracture were subtracted out, success rates concerning pulp vitality increased to 93% and 80% at 5- and 10-year recalls, respectively. This was the first long-term evidence on SCR-SD in permanent teeth available in the literature; however, it was a single-arm clinical trial, with no comparison group.

Bearing in mind that randomized controlled clinical trials are the study design of choice to assess the effectiveness of a given therapy, this evidence was generated more recently. A multicenter, randomized, controlled clinical trial was conducted to compare the effectiveness of SCR-SD and SW in individuals with deep carious lesions ($\geq$1/2 dentin thickness) in permanent molars [58, 78]. It is worth highlighting that this study compared a technique that leaves carious tissue (SCR-SD) and a technique that completely removes carious dentin at the second visit (SW). After 5 years of follow-up [59], success rates in terms of maintenance of pulp vitality were 80% for SCR-SD and restoration in a single visit and 56% for SW ($p < 0.05$). This low success rate observed in the SW group was mainly related to incomplete treatments, in which the patients have not attended the second visit to receive the

final restoration. After a given period, the temporary fillings tend to fail, leading to lesion progression and pulp damage. The comparison of SCR-SD and complete cases of SW showed similar success rates (80% vs. 75%, $p > 0.05$). When it comes to restoration longevity, the 5-year survival analysis showed similar success rates for SCR-SD (79%) and the SW procedure (76%) [79]. These findings confirm that maintaining decayed dentin in the pulpal/axial wall of deep cavities by adopting the SCR-SD technique can preserve pulp vitality without damaging restoration survival in permanent teeth during a 5-year period.

Another study comparing SCR-SD and SW for the management of deep carious lesions (>2/3 of dentin thickness) in permanent teeth was conducted in Egypt, but only the 1-year results have been published so far [56]. During this short-term follow-up period, the authors found similar success rates for both techniques (89.4% for SCR-SD and 84.9% for SW). The estimated mean time free of complications was 23 months for SCR-SD and 18 months for the SW procedure, without significant differences between them ($p > 0.05$). This study also assessed the total cost of both strategies and found a significantly higher total cost for SW than for SCR-SD ($p > 0.05$).

Additional evidence on this topic was provided by a retrospective study that evaluated the longevity of adhesive restorations performed in deep carious lesions in young permanent molars after nonselective caries removal or SCR-SD in a university setting [80]. The survival of restorations reached 57.9% up to the 36-month follow-up, with no difference between the two caries removal techniques ($p > 0.05$).

The systematic review with meta-analysis by Schwendicke et al. [33] showed that for deep carious lesions in permanent teeth, the odds of failure were higher for SW than for SCR-SD (OR 2.25, 95% CI 1.33 to 3.82; 3 studies, 371 teeth; moderate-certainty evidence). However, no difference was observed between these two strategies in the network meta-analysis on the relative effects of different interventions for treating deep lesions.

Based on all the literature discussed in this chapter, it seems clear that there is no evidence to support the need for cavity reopening for further excavation and that SCR-SD may be adopted for the treatment of deep carious lesions in permanent teeth as a single-visit approach.

10.7 Pulp Response to SCR-SD

In addition to clinical studies assessing outcomes such as pulp vitality and restoration longevity, histological studies have been performed to investigate pulp and dentin response to nonselective and selective caries removal [8, 81]. The control (sound) teeth of these studies showed (1) no changes in the dentin/predentin/odontoblast complex; (2) dentinal tubules and odontoblasts layers with normal anatomy and no tertiary dentin or other calcifications; (3) no presence of inflammatory cell accumulations or dilated vessels in the pulp tissues; and (4) no bacteria in the circumpulpal dentin. On the other hand, teeth with deep carious lesion restored after nonselective caries removal presented no pulp inflammation in 28/59, mild

inflammation in 14/59, and irreversible inflammation in 17/59. Regarding the teeth treated with SCR, although all teeth presented inflammation (8/8 [81] and 12/12 [8]), the authors found that: (1) teeth presented no symptomatology and responded within normal limits to thermal and electric tests [8, 81]; (2) teeth presented mild inflammation, with no case of moderate or severe inflammation [8]; (3) tertiary dentin was present in all teeth [8]; (4) bacteria were present in dentin adjacent to the cavity, in the transition between the secondary and the tertiary dentin and, in some cases, in the superficial tertiary dentin [8, 81]. Based on these results, it is possible to conclude that the risk of pulp inflammation is observed with both non-selective and selective caries removal techniques. In addition, it is important to highlight that while almost 30% of teeth treated with nonselective excavation underwent irreversible inflammation and consequently the need for more invasive treatments, no similar cases occurred after SCR. Furthermore, the above-described clinical studies show that less invasive approaches such as SCR-SD may improve patient-relevant clinical outcomes.

10.8 The Role of Cavity Liners After SCR-SD

Cavity liners have been traditionally proposed during the management of deep carious lesions due to several reasons: to reduce the level of contamination, induce tertiary dentin deposition, remineralize demineralized tissues, act as thermal or electric insulator, and protect pulpal cells against irritation stimuli derived from adhesives [82, 83]. Among the used materials, calcium hydroxide cement (CHC), glass ionomer cement (GIC), and hydraulic calcium silicate cements have been used in the clinical practice when the pulpal/axial cavity walls are close to the pulp.

During the decades when decayed tissue was excavated as much as possible and only a thin layer of carious dentin was left over the pulp to avoid its exposure, cavity lining was seen as an essential clinical step during the management of deep carious lesions. However, more recently, the literature has investigated whether the use of cavity liners plays a vital role on pulpal outcomes when applied to deep lesions after conservative caries excavation techniques.

Although the European Society of Endodontology (2019) [37] recommends the use of hydraulic calcium silicate or glass-ionomer cement over the deep dentin in both treatment strategies advocated for the management of deep lesions (SCR-SD and SW), the need for cavity lining in maintaining pulpal vitality has been questioned. A systematic review with meta-analysis by da Rosa et al. [84] investigated whether the use of CHC liner improves the clinical success in the treatment of deep carious lesions. A total of 17 studies were included, of which 15 were conducted in primary dentition and 2 in permanent dentition. Meta-analyses were performed to compare CHC with GIC (data derived from two studies in primary teeth) and CHC with adhesive (data derived from four studies in primary teeth), and no significant differences were observed. The authors concluded that the use of CHC as a cavity liner did not influence the clinical success of treatment for deep lesions; however, the evidence was of moderate to very low quality.

Regarding permanent teeth, the only two studies included in this systematic review [44, 85] reported short-term outcomes (3–4 months of follow-up), and no meta-analysis was performed. Corralo et al. [44] compared lining with CHC, GIC, and an inert material (wax) and found no difference among the tested materials regarding dentin hardening, obliteration of dentinal tubules, decreasing bacterial numbers, and dentin reorganization after 3–4 months of sealing. Pereira et al. [85] compared teeth with and without CHC lining in conjunction with resin-modified GIC restorations. Irrespective of CHC liner use, no difference was found regarding tooth vitality, dentin darkening, hardening, and decreasing contamination after 3 months. Another short-term study not included in the cited systematic review compared the lining with GIC and an inert material for 2 months [86]. The authors found enhanced calcium and phosphorus levels and a better-organized tissue with a more compact intertubular dentin in both groups. They concluded that caries arrestment with dentin reorganization occurs regardless of the lining material placed in contact with the infected dentin.

No long-term study has been performed on permanent teeth. A randomized clinical trial comparing the use of CHC, resin-modified GIC, and adhesive system after SCR-SD reported the 12-month results [87]. Success rates regarding the maintenance of pulp vitality were 96.8%, 96.5%, and 94.6% for CHC, resin-modified GIC, and adhesive, respectively, with no significant difference among groups ($P = 0.81$). A randomized clinical trial, performed by our research group at the Federal University of Rio Grande do Sul, evaluated the effectiveness of indirect pulp protection with CHC or universal adhesive in deep carious lesions after SCR-SD or SW. Over 18 months of monitoring, similar success rates regarding the maintenance of pulp vitality were found (95.5% for CHC and 99.1% for adhesive) (unpublished data).

Lining with CHC has been also compared with mineral trioxide aggregate (MTA) in a randomized clinical trial [88, 89]. Similar success rates were found regarding the maintenance of pulp vitality at the 2-year follow-up (91.7% for CHC and 96.0% for MTA) and at the 4-year follow-up (82.9% for CHC and 86% for MTA).

Based on the available literature on this topic, the adequate cavity sealing is responsible for bacterial reduction and lesion control after SCR-SD. The remaining carious dentin has been seen, itself, as a protective factor for pulp vitality in deep carious lesions. Therefore, using cavity liners does not seem to be important when using conservative caries removal techniques [84, 90, 91].

10.9 Future Perspectives for the Management of Deep Carious Lesions

Current understanding of pulp biology and the pulp response to the release of dentin-bound bioactive growth factors demonstrate that the pulp has a greater regenerative capacity than previously thought [92]. Preserving all or part of the pulp is beneficial, resulting in a less invasive treatment than conventional endodontic

treatment [93], which, in addition to being specialized and costly, removes tooth structure, weakening the tooth.

Pulp preservation or the choice between invasive or more conservative treatment for deep carious lesions depends on the pulpal diagnosis of reversible and irreversible pulpitis, i.e., on the inflammatory status of the pulp. Correlations between histological findings and clinical signs and symptoms have been used to differentiate between stages of reversible and irreversible pulpitis despite limitations [3]. Traditionally, a reversible pulpitis should be treated with a conservative treatment, whereas an irreversible pulpitis should be treated with pulpectomy or tooth extraction [3, 81]. In the same line, Wolters et al. [94] proposed a classification of pulp inflammatory processes with treatment indications:

1. Mild/reversible pulpitis: positive response to the thermal sensitivity test (−20 °C), lasting up to 20 s, with possible sensitivity to vertical and horizontal percussion, but there is no previous history of spontaneous pain. The proposed treatment for these cases is indirect pulp therapy, which provides SCR-SD as a counterpoint to conventional pulpotomy therapy or root canal treatment.
2. Moderate/irreversible pulpitis: symptoms are prolonged response to the thermal test (−20 °C), which can last for minutes, sensitivity to percussion, and presence of spontaneous pain that can be suppressed with pain medication. This may or may not present with thickening of the space of the periodontal ligament and is described as extensive local inflammation confined to the coronary pulp. The therapy indicated for these cases is coronal pulpotomy.

Despite these traditional treatment indications, preliminary investigations have suggested that pulp preservation is possible when vital pulp therapies (such as SCR-SD, IPC, or pulpotomy) are performed in symptomatic teeth [95–98]. Clinical case reports have shown that in some situations of moderate/irreversible pulpitis, where the pulp is conventionally diagnosed as having irreversible inflammation, it can be maintained with clinical and radiographic success [95, 96, 99]. Results of a clinical study by Asgary et al. [93] indicated that vital teeth can be treated with SCR-SD irrespective of the presence of signs and symptoms of pulpitis (mild or moderate). After 1 year of follow-up, the success rates for SCR-SD, direct pulp capping, and partial and total pulpotomy were 95.6%, 88.5%, 85.6%, and 88.7%, respectively, with no statistical difference among groups.

It is important to point out that SCR-SD is a well-established technique for the management of deep carious lesions in teeth with signs and symptoms indicatives of pulp vitality, such as the absence of spontaneous pain, positive response to the cold test, and negative response to percussion, in addition to a periapical radiograph suggesting no pulpal involvement. However, these recent studies including teeth with signs of irreversible pulpal inflammation shed light on this research field. Further studies, mainly long-term randomized clinical trials may broaden the indications of the SCR-SD in the future.

10.10 Concluding Remarks

Based on the aspects discussed along this chapter, it is possible to summarize the contemporary approach for the management of deep dentin carious lesions in primary and young permanent teeth as follows:

- Nonselective caries removal results in a high risk of pulp exposure and is considered overtreatment according to current concepts for caries removal.
- Selective caries removal to soft dentin as a single-visit approach is recommended for the management of deep carious lesions in both primary and permanent dentition.
- There is no reason to reopen the cavity to excavate further, thus eliminating the disadvantages of the stepwise excavation technique related to the need for a second visit.
- The use of a cavity liner after selective caries removal, while not harmful, seems to be an unnecessary clinical step.

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Bioactive Ceramics for Pediatric Dentistry

11

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Contents

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11.1 Bioceramics

Our world is comprised of substances that are organic, metallic, ceramic, or combinations thereof, as depicted in Fig. 11.1. Organic materials have carbon-hydrogen bonds (C-H), which include monomers, polymers, and many other organic compounds; metals are often shiny and good conductors of heat and electricity. Ceramic materials are those materials that are neither metallic nor organic and are often, but not exclusively, oxide compounds. Many ceramic materials are crystalline compounds, but glasses, which are amorphous (non-crystalline), are also ceramics and are often combined with ceramic crystals. Most glasses are based on silica (silicon dioxide, SiO_2), which is distinct from silicone, an organic substance.

Biomaterials are subset of materials (Fig. 11.1) that are used in vivo. Metal, ceramic, and organic compounds may be biomaterials, which are sometimes combined. For instance, composite resin combines organic resins and ceramic filler particles. All dental restorative and prosthodontic materials are biomaterials, and many of them are bioceramics.

Bioceramics may be bioinert, radiopaque, or bioactive (Fig. 11.2) but are best known for being bioinert. Bioinert materials do not elicit a response from the host and do no harm. Alumina and zirconia are examples of inert bioceramics used for prosthodontics, implants, polishing media, and orthodontic brackets. Some bioceramic powders are radiopaque (white on X-ray images), including barium sulfate, bismuth oxide, calcium tungstate, and tantalum oxide. All glass formulas are bioceramics; some glasses are inert, others are inert and radiopaque, and other formulas are bioactive. Bioactive ceramics, the subject of this chapter, do elicit a response in vivo.

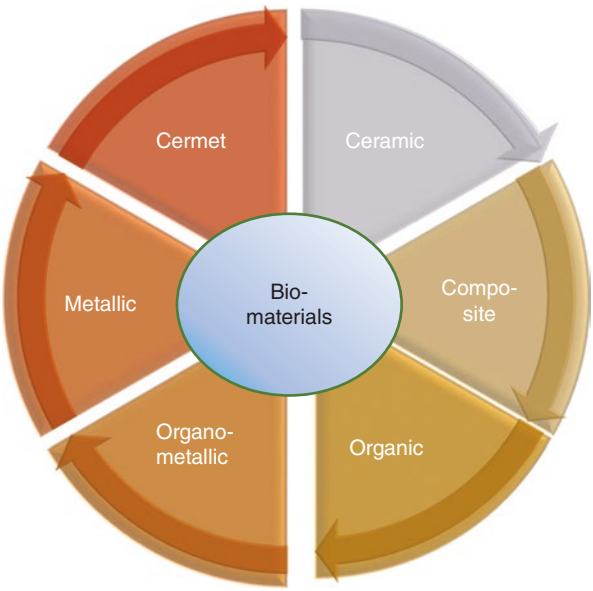

Fig. 11.1 Categories of materials showing the main categories and the subset of biomaterials

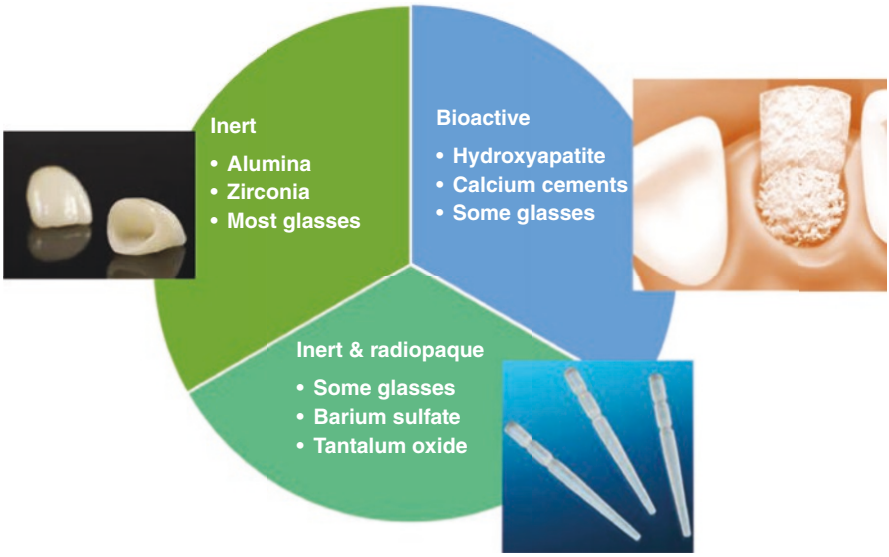

Fig. 11.2 Three categories of bioceramics with examples of crowns, glass fiber posts, and bone grafting material

11.2 Bioactive Ceramics and Biomineralization

Bioactive ceramics provide benefits for healing [1], such as beneficial ion release to stimulate new bone or dentin formation. In this chapter, a more narrow definition of bioactivity is followed as defined by an international standard for surgical materials, ISO 23317:2014: the in vivo formation of a calcium phosphate layer, similar to hydroxyapatite, on the surface of the biomaterial. This international standard has an *in vitro* test for bioactivity using phosphate-buffered saline. This bioactivity has also been denoted as biomineralization. Bioactivity is not limited to biomineralization, which is also the cellular process by which living organisms secrete inorganic minerals [2], but for simplicity, biomineralization is synonymous with bioactivity. Bioactive ceramics, in this context, have two key characteristics: they create a high pH by releasing hydroxide ions, and they release calcium ions in vivo into the body fluids. Body fluids, being supersaturated in phosphate ions, react near the surface of the ceramic where the pH is high, and precipitate a hydroxyapatite-type ($Ca_{10}(PO_4)_6(OH)_2$) layer on the surface of the ceramic, as expressed in Eq. 11.1.

$$10Ca^{+2} + 6PO_4^{-4} + 2OH^- \rightarrow Ca_{10}\left(PO_4\right)_6\left(OH\right)_2 \tag{11.1}$$

[calcium ions + phosphate ions + hydroxide ions] in solution → hydroxyapatite precipitate [crystals].

This precipitation reaction occurs acellularly when bioactive ceramics are placed in simulated body fluid, *in vitro* [3] and in vivo [4]. The precipitated layer may begin as an amorphous calcium phosphate and transform over time to poorly crystalline,

β-type carbonated apatite crystals. The ratio of calcium to phosphate may be lower than 1.67, the ratio in bone. The layer is self-limiting, because when the hydroxyapatite (HA) layer thickens, ion diffusion from the bioactive ceramic is inhibited. When the hydroxyapatite precipitate is formed, the surface of the bioceramic is hidden from the body's immune system and reduces the "foreign body" reaction by which the body identifies, attacks, and attempts to destroy (resorb) the ceramic. The formation of the HA layer precedes a cascade of healing reactions [5, 6] of the pulp or alveolar bone, which are not described in this chapter.

Only a small subset of bioceramics are bioactive, including certain silicate glasses (often denoted as bioglasses), calcium hydroxide, hydroxyapatite, other calcium phosphates, calcium silicate cement, and calcium aluminate cement. The focus of this chapter is on calcium silicate and calcium aluminate cements. These unique cement powders react with water to harden and cause this bioactive reaction in Eq. 11.1.

"Bioactive glasses" were first invented by Hench [7, 8] and contained silica, calcium, and phosphorous oxide but now include similar glasses with magnesium oxide [9] and boron oxide [10] as components. Some bioactive glasses are a component of alveolar bone grafting materials [11] where a coarse (~100 μm) glass powder is implanted, such as in an extraction socket [12]. Bioactive glass and other bone graft materials release ions into the tissue fluids and are slowly replaced by advancing bone tissue. Bone grafting materials rely on micro-, meso- or macroporosity, and their coarse particles serve as bone cell scaffolds [13] for gradual dissolution and resorption of the glass. Both crystalline hydroxyapatite grafting materials and bioactive glass particles are resorbable.

Calcium hydroxide has long been used in dentistry as an antimicrobial [14] medicament that is biomineralizing and stimulates reparative dentin [15]. However, calcium hydroxide is not the best material for pulpotomies for primary teeth, because the histological response has been formation of a deficient, porous reparative dentin [16, 17]. Calcium hydroxide particles gradually form calcium carbonate, which is a bioinert ceramic. Calcium hydroxide is not a cement (it doesn't set nor form a hard layer), unless combined with other substances, such as the resins in Dycal.

Calcium phosphate cements were invented by Chow [18] and are self-setting, bioactive ceramics. Calcium phosphate compounds react to form HA. That is, tetracalcium phosphate, dicalcium phosphate, and dicalcium phosphate dihydrate can gradually dissolve under neutral pH conditions and precipitate HA, amorphous calcium phosphate, or brushite, via self-setting reactions to form a hard mass. The magnesium phosphate cements [19] are similar and are also biomineralizing/bioactive. These cements form HA but are generally slow to set and are considered weak.

The calcium silicate and calcium aluminate cements differ from the bioactive glasses, hydroxyapatite, calcium hydroxide, and calcium phosphate cements. These

calcium cements form a solid mass (set) by reaction with water; that is, they are hydraulic, like calcium phosphate cements. Calcium silicate and calcium aluminate cements are not currently designed to have pores for osseous ingrowth or resorption, unlike the bioactive glasses or calcium phosphate cements; therefore, these solidified cements are usually not resorbable or dissolvable. The cements set within minutes to hours and are bioactive. (See Fig. 11.3 for an ex vivo example showing a hydroxyapatite (HA) layer formed on a calcium silicate cement that had been placed in a root-end filling, soaked in phosphate-buffered saline, and then sagittally sectioned.) The calcium silicate/aluminate cements begin to biomineralize (form HA) acellularly within 30 min. The clinical and histological responses to the calcium silicate/aluminate cements are equal to, or superior to calcium hydroxide [17, 20, 21], perhaps because the cements set and form a matrix and reservoir of hydroxide and calcium ions. This is different from a non-setting paste of calcium hydroxide, a resin cement containing calcium hydroxide, or so-called bioactive resin-modified glass ionomers.

In the last three decades, bioactive calcium silicate and calcium aluminate cements have achieved prominence in pediatric dentistry and endodontics for vital pulp and periapical tissue therapy. This chapter introduces the reader to the unique and beneficial characteristics of bioactive calcium silicate and calcium aluminate cements, explaining the setting reactions, and comparing the dental materials available for pediatric dentistry. From this information, pediatric dentists may make more informed choices for their benefit and the oral health of their patients.

Fig. 11.3 Biomineralization layer (white) on gray calcium silicate cement used in root-end filling. This tooth was filled, soaked in phosphate-buffered saline, and then sectioned

11.3 Bioactive Ceramic Cements

Dental cements include materials to coronally affix prosthodontic or orthodontic devices, either adhesively or via luting (non-adhesive). Dental cements are also used to line a cavity or create an insulating base under a restorative material. The term dental cement is also used for materials that seal root canals with gutta percha. Many compositions of "cements" are used, including the traditional zinc oxide-based cements (phosphate, carboxylate, and eugenolate), glass ionomer, and composite resins. Such cements usually rely on acid-base reactions, and they do contain bioceramic powders but are not bioactive. In this chapter, we focus on the bioactive calcium silicate and aluminate cements that require water for setting and are used in endodontic therapy.

The word "hydraulic" has two meanings: exertion of a uniform pressure by a liquid and materials that set (harden) with water. Hydraulic cements refer to the water-setting ceramics, especially calcium silicate and calcium aluminate compositions. Many non-scientific terms have been used to describe these hydraulic bioactive ceramic cements including mineral trioxide aggregate (MTA), MTA-type materials, tri-/dicalcium silicate-based material/cement, ordinary hydraulic silicate cements, HSC, Portland cement, OPC, PC, calcium silicate cement (CSC), hydraulic cements, hydraulic calcium silicate cement (HCSC), biosilicate, calcium silicate, calcium aluminate, bioceramic cement, BC, and bioactive cement/sealer. Dental product trade names for these bioactive bioceramics often include "MTA," of which ProRoot MTA was the first. Other prominent trade names in this category include Biodentine®, EndoSequence® BC, iRoot®, NeoPUTTY®, MTA Plus®, ProRoot® MTA, and TotalFill® BC.

The earliest publication on calcium silicate cement in dentistry dates from 1878 when Dr. Witte of Germany filled root canals with a locally made, pulverized Portland cement [22]. Portland cement was a new invention at this time. He mixed the cement powder with water and carbolic acid or creosote and filled 25 teeth, with no failures after 1 year. No other mention of using Portland cement in dentistry is known until the twentieth century. Professor Torabinejad at Loma Linda University in California disclosed using Portland cement for dentistry in 1993, based on a specific construction-grade Portland cement that he blended with bismuth oxide powder. Dr. Torabinejad used his calcium silicate cement mixture for endodontic surgery [23] and perforations [24], which were two indications which had been especially problematic for healing. He dubbed his mixture "mineral trioxide aggregate" (MTA) [25] and received a patent with his co-inventor patient, who was an expert in construction-grade Portland cement. The cement of their invention included about 5% iron oxide, which gave the cement a very dark color. His dark-gray, patented composition was commercialized by Dentsply Sirona (USA) in 1997, who manufactured it as ProRoot® MTA. The commercial dental version was a purer, finer powder than the original prototype material from Dr. Torabinejad, having been manufactured by following ISO 13485 and FDA good manufacturing practices. That is, ProRoot MTA did not have the impurities inherent in most construction-grade cements, commonly arsenic, which is restricted (<2 ppm soluble As) in

dentistry. Portland cement is the term used to describe construction-grade, calcium silicate cement and is inappropriate for dental materials, and is not used in this chapter to describe the dental materials. After the gray ProRoot MTA, product, a white version was commercialized and is often denoted as "white" or "tooth-colored" ProRoot MTA in the dental literature. The key to the white ProRoot MTA was reduction of the iron oxide content in the cement. Both ProRoot products were calcium silicate cements blended with bismuth oxide. The ProRoot MTA products were quickly adopted by endodontists, based on the remarkable histological results published for the original material [23, 26]. For instance, cementum and periodontal ligament tissues regenerated over the calcium silicate cement root-end fillings in animals. This healing had not been so pronounced with other root-end filling materials and was greatly appreciated, though at first of unknown mechanism.

Many similar formulas have now been marketed containing calcium silicate cement, many having MTA in their name and other products with new trade names; however, the early imitators of ProRoot MTA all contained calcium silicate cement. In general, the products contain calcium silicate cements of similar but not identical formulas to the cement in ProRoot MTA and a radiopaque powder. Other radiopaque powders are often used, rather than bismuth oxide. Such bioactive ceramic cements are indicated for any pulp, dentin, or alveolar bone-contacting procedure and have become the standard of care for vital pulp therapy [27]. Pediatric dentists use bioactive ceramic cements for pulp capping, lining or base of a cavity, pulpotomy, apexification, resorption, or revascularization. (See the collage of suitable indications in Fig. 11.4, although the indications vary with the products.) Notably, the indications are all within the dentin, not exposed to the oral cavity. This

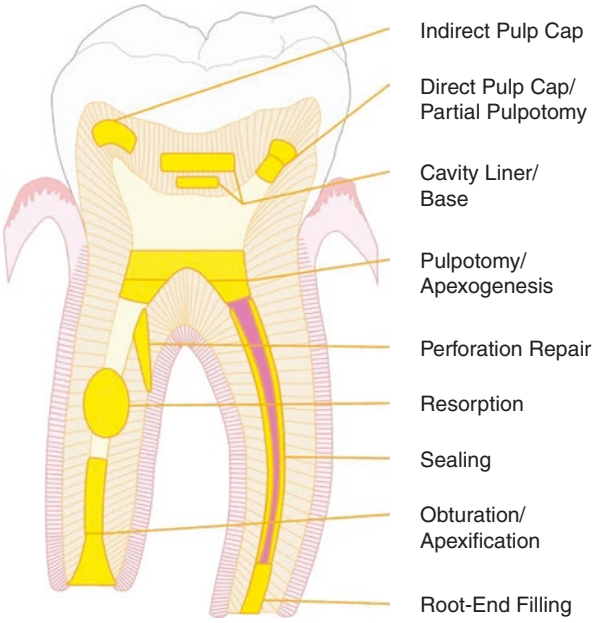

Fig. 11.4 A collage of indications for use of the bioactive ceramic cements, especially for vital pulp therapy. Cement is shown in yellow

limitation is imposed because calcium silicate cement is vulnerable to acids. The calcium silicate cements can be disintegrated by strong acids. Therefore, this cement is unsuitable as a restorative material, where materials are constantly exposed to our acidic diets, unlike the pH-neutral tissue fluids [28]. Obturation after a pulpectomy may be suitable for immature permanent teeth or primary teeth when a successor is absent. However, the current bioactive ceramic cement products are considered non-resorbable and not suitable for primary tooth obturation for fear of disrupting the eruption of the permanent teeth. Despite the versatility in Fig. 11.4 for vital pulp therapy, high-priced bioactive cement products have prevented their universal adoption in pediatric dentistry.

The calcium silicate and calcium aluminate cement powders possess properties not found in most other dental materials. The cement powders set with water, are dimensionally stable, release calcium ions, and form alkaline hydroxides within an amorphous, hydrated cement matrix. Requiring moisture to set is a tremendous benefit for dental applications. Lack of contraction or expansion helps seal the area of the tooth anatomy filled with the cement, unlike other dental materials that often shrink when they set. Most importantly, calcium silicate and calcium aluminate cements release calcium and hydroxide ions from the surfaces of their powders, on contact with moist tissues. These ions create bioactivity and impart antimicrobial action on planktonic bacteria and yeast [29], although insufficient to destroy tenacious biofilms [30]. Calcium aluminate cements have been used in dental restorative materials and crown cements [31, 32]. Calcium aluminate cements have greater acid resistance than calcium silicate cements, a beneficial characteristic for their oral use in acidic and bacterial environments [33]. The pH of the calcium aluminate cements is not quite as high as the calcium silicate cements, but is sufficiently alkaline to produce biomineralization and osteogenic effects [34, 35]. Calcium silicate cement also release silicate ions, which are known to benefit osteogenesis [36], a key phenomenon for healing pulpal or periapical tissue.

11.4 Bioactive Cement Compounds

Phase diagrams are used by materials scientists to understand what compounds (phases) can be manufactured from a particular combination of components. The compositional ranges for the calcium silicate and the calcium aluminate cements are outlined in the partial ternary (3-component) phase diagram shown in Fig. 11.5. A small range of composition is suitable to manufacture the calcium silicate or the calcium aluminate cement phases. The phase diagram shows that some silica may be dissolved in the calcium aluminate cement and some alumina can be dissolved in the calcium silicate cement. Calcium aluminate cement compounds are chemically separate and distinct from the calcium silicate cement region and do not overlap as shown in Fig. 11.5; therefore, the two calcium cements (silicate and aluminate) must be fabricated separately, but may be combined.

Calcium silicate and calcium aluminate bioactive ceramic cements are not naturally occurring; high temperature manufacturing is required. To make these cements,

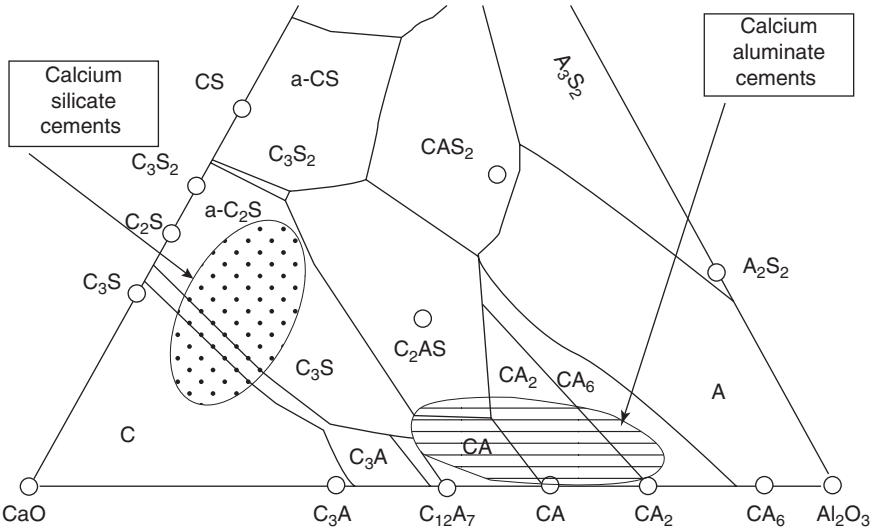

Fig. 11.5 Ternary phase diagram for calcia (CaO, C), silica (SiO_2, S), and alumina (Al_2O_3, A), showing the compositional range for the calcium silicate (area 1) and calcium aluminate cements (area 2)

raw materials are blended, which are ceramic powders, usually containing calcium carbonate, silica, and alumina powders (from varied sources). The blended powders are heated to a peak temperature of about 1500 °C in a kiln. At this high temperature, the raw materials can quickly react to form the cement compounds. The nodules of cement are expelled from the high temperature kiln for quick air cooling, which ensures that the most water reactive phases of cement are maintained. The nodules of cement are called clinker. Minor oxides, such as iron oxide, may be used to control the cement phases and lower the firing temperature. Solution-gelation techniques are an alternative method to manufacture the cement, generally a more expensive route. The fired ceramic cement is ground into a fine powder and sieved via various means. The fine cement powder is placed in a sanitary blender to disperse the cement, radiopaque powder, and any other additive powders evenly. The blended powders may be packaged, or the powder may be mixed with an organic liquid into a paste for placement in syringes. Researchers have speculated on the sources and techniques used for manufacturing the dental cements; however, the compositions and methods are proprietary trade secrets that cannot be easily discerned.

Calcium silicate and calcium aluminate cements discussed above appear to be just two compounds. Chemically, these cements represent six hydraulic ceramic compounds (phases). Calcium silicate cement powders for dentistry are primarily composed of two ceramic compounds: tricalcium silicate (Ca_3SiO_5) and dicalcium silicate (Ca_2SiO_4). These two silicates are known as alite and belite in the commercial Portland cement vernacular, and haturite and larnite in the mineralogical literature, although neither are naturally occurring minerals.

Tetracalcium aluminoferrite ($4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$, ferrite) was present in the original ProRoot MTA, which lowers the firing temperature needed to make calcium silicate cement. Unfortunately, tetracalcium aluminoferrite crystals are black, which darkened teeth immediately where the overlying tissue was thin. The ferrite phase is not considered a necessary component for these bioactive dental cements, so it has been avoided for esthetic reasons. For instance, White ProRoot MTA has low iron content (<1%); consequently, very little of the black ferrite phase is present.

A minor amount of alumina is often intentionally combined with silica and calcia raw materials for making calcium silicate cement to reduce the firing temperature, which is an economic benefit for manufacturing. When alumina is present in larger amounts, tricalcium aluminate ($Ca_3Al_2O_6$ or $3CaO.Al_2O_3$) crystals are formed during firing, concomitant with tri/dicalcium silicate crystals. Tricalcium aluminate is a bioactive cement phase and is present in many of the calcium silicate dental products [37]. Researchers have found the aluminate phase beneficial because of its very rapid hydration, which will accelerate cement setting. The tricalcium aluminate cement compound can be manufactured as a separate powder for addition to calcium silicate cement.

Calcium aluminate cement depicted in Fig. 11.5 is primarily composed of two phases, calcium monoaluminate ($CaO.Al_2O_3$, calcium aluminate) and monocalcium dialuminate ($CaO.2Al_2O_3$, calcium dialuminate), with very little silica. Tricalcium aluminate is usually not included. These two calcium aluminate cement phases react with water to form a hard matrix while releasing Ca^{+2}, $Al(OH)^{-4}$, and OH^- ions at the surface into the tissue fluids, to achieve the same biomineralization (HA precipitation) reaction as the calcium silicate cements. Calcium aluminate cement must be fired separately from the calcium silicate cement formulas, as depicted in Fig. 11.5, showing separate compositional ranges.

11.5 Cement Hydration Reactions

The hydration setting reactions for the bioactive ceramic cement phases are unlike the polymerization reactions used for many dental restoratives. The reactions occur with water and are not catalyzed or activated, unlike light-curing, chemical-curing, or dual-curing dental cements. The hydration reactions show how bioactivity originates. Of the cement phases, tricalcium aluminate sets the fastest, which reacts as in Eq. 11.2.

$$3CaO.Al_2O_3 + 6H_2O \rightarrow 3CaO{\cdot}Al_2O_3{\cdot}6H_2O \tag{11.2}$$

Tricalcium aluminate + water → amorphous hydrated tricalcium aluminate.

The reaction product of Eq. 11.2 is a hydrated gel of calcium aluminate. The rapid hydration of tricalcium aluminate phase speeds setting of calcium silicate cements; therefore, some researchers have intentionally added more tricalcium aluminate powder [38]. Tricalcium aluminate releases heat as it hydrates. In a tooth, the heat is easily mitigated, and enough tissue fluid is available to continue hydration.

However, calcium sulfate is sometimes used to modulate the setting of the tricalcium aluminate crystals. Calcium sulfate reacts with water and the tricalcium aluminate to form the intermediate product of ettringite ($Ca_3Al_2O_6.3CaSO_4.32H_2O$) or monosulfate ($Ca_3Al_2O_6.CaSO_4.12H_2O$), evolving less heat. This mitigation of rapid hardening is similar to the use of calcium sulfate dihydrate in alginate to slow its setting time.

The ferrite cement phase also undergoes rapid hydration, as noted in Eq. 11.3. The reaction products include a hydrated cement of calcia and alumina and release alkaline iron hydroxide.

$$4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3 + 19H_2O \rightarrow 2\left[2CaO{\cdot}Al_2O_3.8H_2O\right] + 2Fe\left(OH\right)_3 \quad (11.3)$$

Tetracalcium aluminoferrite + water → amorphous hydrated ferrite + iron oxide hydrate.

Calcium sulfate and calcium oxide are also used to mitigate overly fast setting of the ferrite, similar to tricalcium aluminate. Ferrite may also form complex calcium-alumino-ferric-sulfate hydrates, such as $3CaO{\cdot}(0.5Al_2O_3{\cdot}0.5Fe_2O_3){\cdot}3CaSO_4{\cdot}32H_2O$, $Ca_2(Al,Fe)_2O_5$, or $4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$ [39].

The main hydration setting reactions for calcium silicate cement phases are shown in Eqs. 11.4 and 11.5.

$$2\left[Ca_3SiO_5\right] + 7H_2O \rightarrow 3CaO{\cdot}2SiO_2{\cdot}4H_2O + 3Ca\left(OH\right)_2 \quad (11.4)$$

Tricalcium silicate (alite) + water → amorphous calcium silicate hydrate + calcium hydroxide.

$$2\left[Ca_2SiO_4\right] + 5H_2O \rightarrow 3CaO{\cdot}2SiO_2{\cdot}4H_2O + Ca\left(OH\right)_2 \quad (11.5)$$

Dicalcium silicate (belite) + water → amorphous calcium silicate hydrate + calcium hydroxide.

After a brief induction period, the tricalcium silicate phase hydrates, faster than the dicalcium silicate phase. Both calcium silicate phases react to form an amorphous hydrated calcium silicate ($3CaO{\cdot}2SiO_2{\cdot}4H_2O$) concurrently releasing calcium hydroxide, known as portlandite in cement literature and occasionally in dental literature [40]. Dicalcium silicate crystals gradually hydrate, which decreases the porosity of the setting cement. Setting may take minutes to hours, depending on the composition and proportions of the phases. The compressive strength increases over about 4 weeks; however, most of the strength is developed in less than a week.

The calcium aluminate cement phases, calcium aluminate ($CaO.Al_2O_3$) and monocalcium dialuminate ($CaO.2Al_2O_3$, calcium dialuminate), have interesting hydration reactions that vary with temperature from 0 to 100 °C [41]. Fortunately, the body maintains a constant temperature for the hydration reactions, which are expressed in Eqs. 11.6 and 11.7 for the calcium aluminate ($CaO.Al_2O_3$) and calcium dialuminate ($CaO.2Al_2O_3$) cement phases.

$$3\left[CaO.Al_2O_3\right] + 12H_2O \rightarrow 3\left(CaO\right){\cdot}Al_2O_3{\cdot}6\left(H_2O\right) + 2\left[Al_2O_3.3H_2O\right] \quad (11.6)$$

Calcium aluminate + water → amorphous calcium aluminate hydrate + aluminum hydroxide.

$$3\left[\mathrm{CaO}\left(\mathrm{Al_2O_3}\right)_2\right]+21\mathrm{H_2O}\rightarrow 3\left(\mathrm{CaO}\right)\cdot\mathrm{Al_2O_3}\cdot 6\left(\mathrm{H_2O}\right)+5\left[\mathrm{Al_2O_3}.3\mathrm{H_2O}\right] \quad (11.7)$$

Calcium dialuminate hydration + water → amorphous calcium aluminate hydrate + aluminum hydroxide.

Calcium aluminate cements, like the calcium silicate cement phases, create a high pH environment and release calcium ions, which are the prerequisites for biomineralization (bioactivity/apatite formation). Some investigators have combined these calcium aluminate phases with calcium silicate compounds to combine the benefits of the silicate ion release for osteogenesis and the acid resistance of calcium aluminate cement for dentistry.

Pozzolanic cement, Roman cement, is based on the reaction of silica with calcium hydroxide or calcia (CaO). With water, the ceramics react as in Eq. 11.8, where the proportions of the hydrated calcium silicate are indefinite (m, x, and n) and depend on the composition. The silica and calcium hydroxide react with water, forming a hard hydrated calcium silicate phase cement that differs from the tri-/dicalcium silicates.

$$\mathrm{SiO_2}+\mathrm{Ca}\left(\mathrm{OH}\right)_2+\mathrm{mH_2O}\rightarrow\left(\mathrm{CaO}\right)_x\,\mathrm{SiO_2}.\mathrm{nH_2O} \quad (11.8)$$

[silica + calcium hydroxide + water → hydrated calcium silicate].

For construction, calcium silicate cement (Portland cement) supplanted pozzolanic cement in the 1800s, because Roman cement doesn't have the strength of the calcium silicate cements. Two dental products have been advertised as "fast-setting, mineral trioxide aggregate–derived pozzolan cements," but the components are not known; they may include fine, amorphous silica and calcium hydroxide. The pozzolanic hydration reaction may cause shrinkage [42], an undesirable effect for dental cements. No clinical or physical benefits have been published for the pozzolanic dental cements [43].

The calcium aluminate, calcium silicate, and pozzolanic cements react with water by surface hydration of the powder particles, which release calcium and hydroxide ions into the tissue fluids. These ions enable the formation of HA on the cement surface in vivo, which is herein denoted as bioactivity.

11.6 Pediatric Bioactive Ceramic Dental Cements

Many bioactive cement products are available for pediatric use, and some are listed in Table 11.1. Various salient properties should be considered for choosing a bioactive cement product including the ones discussed below: indications, composition, format, packaging, and product characteristics.

Table 11.1 Bioactive ceramic cement dental products

Product name (alphabetical order)	Manufacturer or distributor	Format	Unit/ multi-dose?	Radiopaque component	% Cement in powder	$CaSO_4$, $Ca(OH)_2$, or $CaCO_3$	SiO_2	Other
Original MTA	Courtesy of Dr. M. Torabinejad	Powder/water	Multi	Bi_2O_3	70	3.7	1.7	2.2
BC Root Repair Putty	Innovative Bioceramix, distributed by Brasseler, FKG Dentaire, and EdgeEndo	Single paste	Multi	ZrO_2, Ta_2O_5	63	3.2		
BC Fast-Set Putty		Single paste	Multi	ZrO_2, Ta_2O_5	55	7.7		
BC Root Repair-jar		Single paste	Multi	ZrO_2, Ta_2O_5	59	8.0		
BioAggregate	Innovative Bioceramix	Powder/water	Unit	Ta_2O_5	88	5.4		
Biodentine	Septodont	Powder/liquid	Unit	ZrO_2	83	13.7		
Bio-C Repair	Angelus	Single paste	Multi	ZrO_2	37			
BIOfactor MTA	Imicryl	Powder/liquid	Multi	Yb_2O_3	Unknown			
BioMTA	Diadent	Powder/liquid	Unit	ZrO_2, Yb_2O_3, $CaTiO_3$	40	9.1		
BIO MTA+	Cerkamed	Powder/liquid	Multi	ZrO_2	Unknown			
CEM	Bionique	Powder/water	Multi	$BaSO_4$, ZrO_2, ZnO	83	4.3		
Channels MTA	Angelus/Schein	Powder/liquid	Multi	Bi_2O_3	Unknown			
CPM Endo	Egeo	Powder/liquid	Multi	Bi_2O_3, $BaSO_4$	78	14.8		
e-MTA	Kids-e-dental	Powder/water and gel	Multi	Undisclosed	Unknown			
EndoBinder	Binderware	Powder/liquid	Multi	$CaZrO_3$, ZrO_2	80			
EndoCem MTA	Maruchi	Powder	Unit	Bi_2O_3	36	42.0		
EndoCem Zr	Maruchi	Powder/water	Unit	ZrO_2	36	45.4	2	1.1

(continued)

Table 11.1 (continued)

Product name (alphabetical order)	Manufacturer or distributor	Format	Unit/ multi-dose?	Radiopaque component	% Cement in powder	$CaSO_4$, $Ca(OH)_2$, or $CaCO_3$	SiO_2	Other
Endo-PASS	DEI Italia	Powder/water	Unit	$BaSO_4$	73			
Harvard MTA	Harvard	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
Master-Dent MTA	Dentonics	Powder/gel	Multi	Bi_2O_3	77	1.8		
Medcem	Medcem	Powder	Unit	None, or ZrO_2	70	6.7		
MM-MTA	MicroMega	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
MTA Caps	Acteon	Dual-compartment capsules	Unit	$CaWO_4$	48	18.3	0.4	
MTAFlow	Ultradent	Powder/gel	Multi	Bi_2O_3	73	2.0		
MTAFlow (White)	Ultradent	Powder/gel	Multi	Ta_2O_5	72	2.2		
MTA gray or white	Angelus	Powder/liquid	Multi	Bi_2O_3 or $CaWO_4$	83	5.6		6.7
MTA HP	Angelus	Powder/liquid	Unit	$CaWO_4$	81			
MTA Plus	Prevest Denpro	Powder/gel	Multi	Bi_2O_3	77	1.8		1.7
MTA+	Cerkamed	Powder/water	Multi	Bi_2O_3, ZrO2	67	2.0	14	
MTA White	Angelus	Powder/water	Multi	$CaWO_4$	92			
NeoLINER LC[a]	NuSmile	Single-paste resin	Multi	Undisclosed	Unknown			
NeoMTA 2	NuSmile, Avalon Biomed	Powder/gel	Multi	Ta_2O_5	63	0.6	1.2	
NeoMTA Plus	NuSmile	Powder/gel	Multi	Ta_2O_5	72	1.3	1.6	
NeoPUTTY	NuSmile, Avalon Biomed	Single paste	Multi	Ta_2O_5	47	1.0		

OliMTA	Olident	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
Orbis MTA	Orbis	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
Ortho MTA	bioMTA	Powder/water	Unit	Bi_2O_3	Unknown			
PD MTA	Produit Dentaire	Powder/water	Unit	Bi_2O_3, $BaSO_4$	50	36.4		4.7
Oxford MTA	Oxford scientific	Powder/liquid or dual-compartment capsules	Multi or unit	Undisclosed	Unknown			
ProRoot MTA (gray)	Dentsply Sirona	Powder/water	Unit	Bi_2O_3	76	3.6		
ProRoot MTA (white)	Dentsply Sirona	Powder/water	Unit	Bi_2O_3	80			
ReMTA	Dental Solutions Israel	Powder/water; single paste, and dual paste	Unit and multi-dose	Bi_2O_3	Unknown			
RetroMTA	bioMTA	Powder/water	Unit	ZrO_2, $CaZrO_3$	66			
Smart MTA	Sprig	Powder/water	Unit	ZrO_2	73			
TheraCal LC[a]	Bisco	Single-paste resin	Multi	$BaZrO_3$	78	5.5		
TheraCal PT[a]	Bisco	Dual-paste resin	Multi	$BaZrO_3$, YbF_3	20	33.8		
Trioxident	Vladmiva	Powder/water	Unit	ZrO_2	79			
Vivid Root MTA	Pearson dental	Dual-compartment capsules	Unit	Undisclosed	Unknown			
Well-Root PT	Vericom	Single paste	Multi	ZrO_2	57	1.9		

[a]Resin-based
Blanks indicate the compound is not present

11.6.1 Indications

All the products in Table 11.1 are suitable for pulpotomies and other vital pulp procedures except the resin-containing cements: TheraCal® LC is only indicated for pulp capping, NeoLINER™ LC is indicated for lining a cavity preparation (not pulp capping), and TheraCal PT is limited to pulpotomies. EndoCem Zr is not indicated for use as a base. Biodentine is the only material that is used as a temporary restorative for up to 6 months. No product is specifically indicated for revascularization.

The resin-based materials contain monomers with dispersed bioactive cement powders; however, they have not been as clinically successful as bioactive cements without resin [44, 45], although they are reasonably priced. Resin-containing products are more suitable for indirect pulp capping [46]. TheraCal PT may be more biocompatible than TheraCal LC, but not as biocompatible as MTA Angelus [47], a non-resin containing bioactive cement. The clinical performance of TheraCal PT in clinical tests of pulpotomies has not been tested, although a trial is underway (NCT04167943).

No clinical superiority has been established for any other of the bioactive ceramic cement products. The amounts of the cement vary in the products, as discussed below, but a lower limit for cement content has not been established. Nor has an "optimum cement composition" been determined, based on the individual cement phases discussed above. In fact, commercial, construction-grade, Portland cement has been considered as clinically effective as the dental bioactive bioceramic, despite the construction-grade cement being coarse radiolucent, tending to wash out and setting slower. However, using non-dental cement is ill-advised at best. Other than bismuth oxide (discussed below), no superiority has been established for any radiopaque additive, nor for any minor additive.

11.6.2 Composition

The composition of the bioactive ceramic products has been confusing for dentists because of the various advertising claims and non-sensical, non-chemical product names that are used, as mentioned previously. Furthermore, the cement compounds were misidentified in the first publication of MTA's [37] composition. Clinicians can identify some components of the bioactive ceramic products by examining the Safety Data Sheets (SDS) for a product, and reading the dental literature. The SDSs should reveal any hazardous components but are often non-specific and incomplete as to the composition.

Dental publications about the composition of these bioactive ceramic cement products have often been based on scanning electron microscopy (SEM), including atomic analysis using energy-dispersive spectroscopy (EDS), a.k.a. energy-dispersive X-ray spectroscopy (EDX or XEDS) [48]. The SEM/EDS technique can image the product, before or after setting, and can identify the major atoms present. For instance, calcium and silicon can be identified by SEM/EDS, but whether the phases were dicalcium silicate or tricalcium silicate must be inferred because SEM/

EDS equipment cannot identify the ceramic phases (compounds). Another problem with the EDS technique is that the spectra represent a sample deeper and wider than the electron beam, which makes EDX quantitative analysis imprecise, particularly if a material is being examined inside a tooth. Porosity also interferes with EDS spectra; therefore, the spectra may not represent the composition where the electron beam is "pinpointed." Energy dispersive spectra is a "rougher" material science tool for chemical analysis compared to other methods, such as wavelength dispersive X-ray spectroscopy (WDS), performed with an electron microprobe, but less commonly used by researchers. X-ray fluorescence (XRF) is also used to analyze the elements present in materials and can measure trace elements present in parts per million, a much more precise elemental analysis than EDS. XRF atomic results are converted to oxides using software, but XRF requires the destructive analysis of a larger, non-microscopic sample and does not reveal the compounds present. X-ray diffraction is used by materials scientists to determine the crystalline phases (compounds), such as the cement phases discussed before. X-ray diffraction may be performed with powders or pastes, but does not identify trace metals, organic compounds, amorphous materials, or crystalline phases present at less than about 1%. No one analysis technique is a comprehensive tool, but a combination of analyses is useful for understanding materials and their behavior for its presentation in the dental literature.

X-ray diffraction was used by this author to compare the bioactive bioceramics powder, paste, and resin products suitable for pediatric dentistry. The results in Table 11.1 also include some data from the dental literature, the gray literature, and the companies' safety data sheet (SDS) for products that were not available for analysis. The total amount of the cement phases varied from 36 to 92% by weight, and the cement phases were mostly tricalcium silicate and dicalcium silicate. Most products contained more tri- than dicalcium silicate; however, EndoCem MTA and EndoCem Zr contained only dicalcium silicate. Aluminate cement phases were identified in Angelus MTA HP, CPM Endo, EndoBinder, BioMTA, MTA +, MTA Caps, NeoPUTTY, PD MTA, ProRoot MTA, Sprig SmartMTA, RetroMTA, TheraCal PT, and Trioxident. Two products contained the calcium aluminate cement phases ($CaO.Al_2O_3$ or $CaO.2Al_2O_3$): NeoPUTTY and EndoBinder.

Some products contained significant amounts of calcium oxide, hydroxide, or calcium carbonate. The calcium compounds are not cement phases and do not add radiopacity. Calcium sulfate was present in some products, perhaps for setting control or calcium release. Other minor components were identified by XRD: magnesia, silica, calcium hypophosphite, and calcium chloride. Amorphous or low-crystallinity components may be present in the powders or pastes including fumed silica, chitosan, cellulose, and various clays; these compounds cannot be discerned by X-ray diffraction, as they would only appear as broad humps, not sharp peaks in the X-ray diffraction spectra. However, these additives have been mentioned in patents for such materials, used to thicken and stabilize pastes for better handling. These non-cement components may be included to augment calcium ion release, speed up setting, increase strength, or reduce the firing temperature required for manufacturing the cement (e.g., MgO).

11.6.3 Radiopacity

Diverse ceramic powders have been blended into the bioactive ceramic cements for radiopacity (Table 11.1), which are, in order of increasing molecular weight, zinc oxide (81 g/mol), zirconia (123 g/mol), calcium zirconate (179 g/mol), ytterbium fluoride (230 g/mol), barium sulfate (233 g/mol), barium zirconate (277 g/mol), calcium tungstate (288 g/mol), ytterbium oxide (394 g/mol), tantalum oxide (442 g/mol), and bismuth oxide (465 g/mol). Newer bioactive cement tend to contain more radiopaque powder than the 20 weight percent bismuth oxide in the ProRoot MTA patent. The radiopacities of the bioactive ceramic cements vary from about 1 to 8 mm of equivalent aluminum for pediatric bioactive cements, when tested per the standard method of ISO 13116. For reference, dentin has a radiopacity equivalent to about 1 mm of aluminum. Resin-containing products, such as TheraCal LC and PT, have the lowest radiopacity (~1 mm equivalent Al) [49].

Antibiotics or injury may discolor teeth, but the gray and white ProRoot MTA products also discolored teeth. Discoloration can be immediate from using a gray-colored powder such as the original, dark gray, ProRoot MTA, containing the ferrite cement phase. Surprisingly, the white ProRoot MTA also caused gradual, delayed discoloration, especially in the thinner, primary teeth [50]. The primary cause of discoloration has been traced to the inclusion of the bismuth oxide powder used for radiopacity. When exposed to light and certain chemicals, Bismuth oxide forms darker-colored bismuth compounds, such as bismuth subcarbonate, $Bi_2O_2(CO_3)$, sodium bismuthate, or reddish Bi_2O_{4-x} [51], when exposed to light and certain chemicals. The color change is caused by bismuth ions that transform under oxidation or exposure to light from trivalent (Bi^{+3}) to pentavalent (Bi^{+5}). The darkening of the bismuth oxide in the bioactive cements was not esthetic, but does not compromise the dental cements' safety or efficacy [50]. Although the original ProRoot MTA products continue to contain bismuth oxide, most newer products do not contain this radiopaque component. Notably, many products in Table 11.1 have "MTA" in their trade name, but do *not* contain bismuth oxide. Therefore, not all "MTA" products discolor, despite some generalizations made in the literature. The only common characteristic of the so-called MTA products is the presence of calcium silicate cement.

11.6.4 Pastes and Resins

Another tool of materials scientists is thermogravimetric analysis (TGA). Using this technique, a small sample is gradually heated to about 1000 °C, while its weight change is monitored. TGA was used to measure the amount of organic liquid or resin present in some of the single- and dual-paste products (Table 11.2). About 15 to 30% organic liquid, such as glycols of various molecular weights, are used in some cement pastes that set in vivo. The EndoCem paste is known to contain another liquid, dimethyl sulfoxide (DMSO). For all these paste products, the organic liquid diffuses from the cement paste *in vivo*, while water from tissue fluids migrates into the cement pastes to cause setting. Resin-containing pastes are different because

Table 11.2 Bioactive ceramic cement dental paste products for pediatric dentistry

Product name (alphabetical order)	Manufacturer or distributor	Format	% Organic liquid	% Resin
BC Root Repair Putty	Innovative Bioceramix, distributed by Brasseler, FKG Dentaire, and EdgeEndo	Single paste	16	
BC Fast-Set Putty		Single paste	15	
BC Root Repair-jar		Single paste	19	
Bio-C Repair	Angelus	Single paste		
NeoLINER LC[a]	NuSmile	Resin		Unknown
NeoPUTTY	NuSmile, Avalon Biomed	Single paste	20	
TheraCal LC[a]	Bisco	Resin		33
TheraCal PT[a]	Bisco	Dual-paste resin		37
Well-Root PT	Vericom	Single paste	21	

[a]Resin-based

resins remain in place after setting. Polymerized resins control the release of the cement ions that are embedded in the resins. As a result, bioactivity (ion release) is lower in these resin products. Resin products contain about 35% monomer.

11.6.5 Format

The formats of the bioactive ceramic cement products vary widely, with some more convenient and others more affordable [27]. The products contain bioactive cement powder formatted as (1) powder and liquid that the clinician mixes into a viscous paste, (2) single pastes, or (3) resin-based materials (that contain some bioactive cement particles). Powder/liquids products set because the water in the liquid starts the setting; these products may be single or multi-dose in format. Pastes set because tissue fluids provide water for setting. Well-Root PT is a single-dose, single paste in a compule-type dispenser, but usually pastes are sold in multi-dose syringes. Resin materials set because the matrix is cured, but the cement is not set except on the surface where it is exposed to tissue fluids. The formats of these bioactive ceramic cement products are important to clinicians for convenience, speed of treatment, and cost. Table 11.1 lists many bioactive ceramic cement products for pediatric dentistry, designating the format as single or multi-dose.

The first bioactive bioceramic cement kit, ProRoot MTA, contained foil sachets of powder and ampoules of water for clinicians to mix as individual doses. The sachets contain 0.5 g, much more than needed for a pediatric dose (<0.1 g), and resealing the sachets is not possible. This foil sachet format has been copied for products such as RetroMTA, PD MTA, Trioxident, and reMTA (Fig. 11.6a) and the original BioAggregate product.

Unique capsules of powder have been offered as unit doses by Septodont, Medcem, and Angelus, companies containing 0.7, 0.35, and 0.19 g (Fig. 11.6b). Biodentine (Septodont) and Angelus capsules are plastic, whereas Medcem MTA and Endo-PASS MTA are sold in gelatin capsules. Septodont Biodentine® and Angelus MTA HP kits include ampoules of water-based liquid containing a salt and polymer (calcium chloride and an unidentified carboxylate polymer) to impart faster setting and higher strength [52]. The dentist adds the Biodentine liquid dropwise to the powder in the capsule; then the capsule must be triturated to mix. 0.7 g of powder per capsule of Biodentine is large for one tooth but useful when many

Fig. 11.6 (**a**) Unit-dose packaging of bioactive ceramic cement powders in foil sachets. (**b**) Unit-dose packaging of bioactive ceramic cements in capsule or vials, used for powder or liquid or both. Some products include foil pouches; others use plastic packages. The centrifuge for mixing OrthoMTA is shown in the lower right-hand corner. (**c**) Dual-compartment capsule products for powder and liquid. (**d**) Multi-dose kits of bioactive ceramic powder and liquid. (**e**) Paste forms of bioactive cements that self-set. (**f**) Resin-based materials that set by light curing or dual curing

Fig. 11.6 (continued)

Fig. 11.6 (continued)

Fig. 11.6 (continued)

Fig. 11.6 (continued)

Fig. 11.6 (continued)

teeth need treatment, such as pediatric pulpotomies [27], or as a temporary restorative. MTA HP powder and liquid are hand-mixed on a glass or impermeable pad. The Medcem MTA and Endo-PASS MTA gelatin capsules tend to be brittle and messy when opened; they must be mixed with a clinician-supplied liquid. Other unit-dose packaging options for the bioactive cement powders have included plastic "centrifuge" vials, often with a 0.3 g dose as shown in Fig. 11.6b. For the OrthoMTA product, the dentist mixes with water in the vial and then uses a battery-operated centrifuge for mixing. These unit-dose powder and liquid capsules and vials are often, but not exclusively, sold in protective foil pouches to prevent the ingress of water. Some of the vials of water-based liquid are also packaged in foil pouches, some resealable, others not.

Dual-compartment capsules for trituration of a unit-dose are shown in Fig. 11.6c. These capsules are similar to amalgam or glass-ionomer unit-dose capsules and usually provided in foil pouches. The capsules have two compartments: one for the cement powder and one for water or a water-based liquid separated by a membrane of foil. The capsules are "activated" by the dentists compressing a plunger and then triturating the capsule. The wet cement mixture is dispensed by opening the capsule or using a capsule product that has a dispensing tip. Dual-compartment capsules for trituration usually contain 0.3 g of powder and water and have been sold by Acteon, Harvard, Micro-Mega, Orbis, Oxford, and Pearson. Usually, two capsules are packaged in a foil pouch. From the similarity of the capsule products, one may surmise that some are private labeled. In 2022, Biodentine introduced their unique design of a single-dose, dual-compartment capsule and a special mixer. The cost of dual-compartment capsules is higher per dose or per gram, compared to hand-mixed and multi-dose products.

Multi-dose powder/liquid kits of bioactive cements (Fig. 11.6d) began with the first Angelus MTA products, gray and white, which included a bottle of cement and a dropper bottle of water. The advantage of multi-dose bottles is the clinical control, i.e., one has to dispense only what is needed. Mixing a powder and liquid requires a bit of skill and familiarity but allows a clinician to customize the viscosity and handling. Variations in the powder-to-liquid ratio have been explored; a weight ratio of 3 to 1 is most common and often used in research tests, but ratios have been evaluated from 2:1 to 4:1 [53]. Higher powder-to-liquid ratios increase the viscosity of the mixed cement, shorten the setting time, and lead to a higher strength cement. Hand, ultrasonic, and trituration mixing have been evaluated for their effects on mixed MTA Angelus, but only small differences were observed. The relatively high cost of the calcium silicate cement products has made mixing an issue, because of the potential for waste of mixed, unused cement paste, but savvy assistants can avoid waste with a little practice. Water-based gel is included in some of the multi-dose kits shown in Fig. 11.6d for products including MTA Plus®, NeoMTA Plus®, NeoMTA®2, Masterdent® MTA, MTAFlow® (white and gray), and e-MTA products. Water-based gels are higher in viscosity (thicker) than water, from which one surmises the gels contain water-soluble polymers or organic liquids. The gels improve the handling, ease of placement, and washout resistance of the mixed cements [54]. Some multi-dose products include water (CEM) or a salt solution (BioMTA +).

Paste products (Fig. 11.6e) that set in vivo are the latest format of the bioactive ceramic cements. Such single-paste products may be denoted as premixed pastes or putty and have a high viscosity that is a thick, putty-like, consistency similar to IRM® and quite suitable for pediatric dental procedures. These pastes are available either in syringes or a small "pot." The syringes have had superior shelf life compared to one, expensive brand sold in a small jar [55]. Only Well-Root PT paste is sold in compules for individual doses. For these pastes, the cement powder has been blended into a water-free, organic liquid. Being water-free, the cement doesn't set in the syringe or compule. However, when the paste is placed in vivo, water from the body tissues diffuses into the paste and causes setting of the cement, while the organic liquid diffuses into the body tissues; no light activation and no catalyst are needed. These pastes are very washout resistant and provide a very fast convenient dispensing option. These putty-like pastes set over a few hours because the body has to supply the water for setting. These paste products of bioactive cements are convenient and economical for dispensing, with little waste; however, the pastes cost more per gram than the powder-liquid systems.

11.6.6 Packaging Materials

Clinicians should be aware that all packaging materials are imperfect barriers and usually control the shelf life of products. Water can permeate all barriers to powder packaging, including foil and plastics, although multi-layered foil/polymer resealable pouches are superior. Even glass bottles may allow water to enter through the plastic cap and its seal. Some of these bioactive cement powders are packaged in foil sachets (small pouches) for powder; other products package the cement powder in glass or plastic bottles, capsules, or vials as noted before. Desiccants in the bottles of powder are used for NeoMTA2 powder, MTAFlow, and the MasterDent products to prolong the powders' shelf life. When water permeates the bioactive ceramic cement powder packaging, the setting time is lengthened; handling is degraded by partial hydration, making it granular (crumbly); and the set cement is weaker. This problem is worse for the foil sachets which cannot be resealed, such as the one used for ProRoot MTA.

Evaporation from the unit-dose containers of water-based liquid is also important. Over the shelf life of the product, usually 2 to 3 years, evaporation of water will occur from the unit-dose liquid containers, which increases the powder-to-liquid ratio of unit-dose products. Also, it is difficult to precisely package weights of powder in vials, ampoules, or pouches. Liquid dose packaging can be more accurate than powders, but the evaporation through the packaging can reduce the amount of liquid over time. These minor variations can be detectable to clinicians. Slightly thicker mixtures may be detected when mixing unit-doses of powder and liquid that are nearing their expiration date. Also, select dental materials are sold as sterile, which must be marked as sterile. Most dental restoratives or cements are not sterile. Some authors have believed that the bioactive cement products are sterile or have sterile liquid components; however, sterile products are always marked as sterile.

Combining all these factors, these bioactive ceramic cement products have a shelf life of 2–3 years, as do most dental products.

11.7 Cement Product Characteristics

The first calcium silicate cement products (ProRoot MTA and MTA Angelus) were clinically effective, but tended to wash out, had a long setting time (>2 h), caused tooth darkening, and had high cost (~$50/g). The products were maligned as "just expensive Portland cement." Newer and modified products have moderated these issues. The current hydraulic, bioactive ceramic cements have easier handling and faster setting time, do not darken teeth, and have lower cost while maintaining excellent clinical performance. These product improvements have been made possible by manufacturers making finer particles sizes of powders, modifying the liquids for mixing, adding some other ceramic powders, inventing paste forms, and incorporation of non-bismuth oxide radiopaque ceramic powders, all amid international competition. The current properties of various bioactive cements for pediatric dentistry are discussed below.

11.7.1 Handling

The original MTA prototype and ProRoot MTA was considered "sandy" in consistency, that is, the powder was coarser than powder products to which dentists are accustomed. Manufacturers have improved the powders, making them very fine, eliminating the coarse powders. Newer, more radiopaque powders are also very fine, with some powder particles in the nanoparticle range (<0.1 μm, <100 nm). Finer particles contribute to easier handling, better cohesion when mixed with liquids, and faster setting/hydration. The newer, water-based solutions and water-based gels create benefits of washout resistance, easy handling and placement, a more desirable "plastic" consistency, and faster setting of the bioactive cements. Many of the bioactive bioceramic cements can be mixed to a dough-like consistency that can be picked up with a small instrument like amalgam carriers, or the small "MTA" carriers. (See Fig. 11.7.) These improvements eliminate the need for special "MTA" instruments for clinical placement. The paste products streamline the application with no need for mixing; however, the viscosity is not usually adjustable, unless extra liquid or powder is supplied.

Practice is often needed to economically mix the bioactive, powder-liquid, multidose, cement products. Impermeable pads are a necessity; otherwise, the pad absorbs the liquid and creates problems; glass palettes are especially suitable. A medium-stiffness metal spatula is best to ensure the powder and liquid are well mixed; plastic spatulas are not well designed for mixing these very fine powders. Problems with mixing proportions can arise because scoops and drops vary among users. When too much powder is added to the liquid, the mixture is dry and crumbly; however, more liquid should be added in small increments, usually less than a

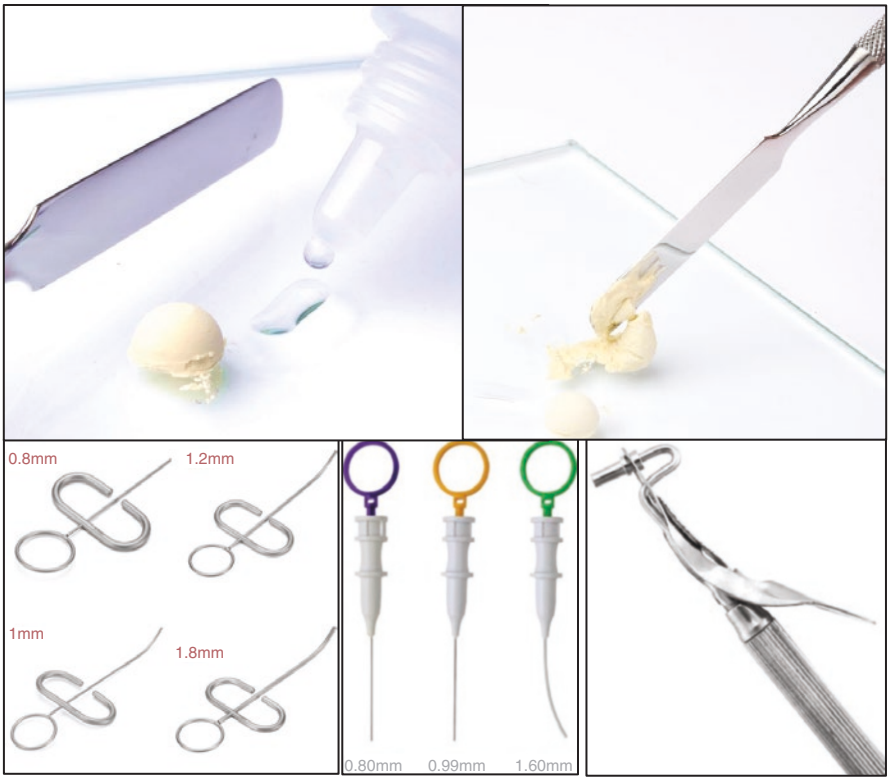

Fig. 11.7 Instruments for mixing and placing bioactive bioceramics having a putty-like consistency

drop. When too much liquid is added to the powder, the mixture is unmanageable, thin, and slow to set. When the mixture is thin, the tendency is to add more powder. If time permits, the thin mixtures can be spread out to allow the water-based liquid to evaporate and thicken the cement. Very little bioactive cement is needed clinically, so any increment of powder added to a thin paste should be very small, less than the scoop provided by a manufacturer. Adding powder can create a lump of cement that is much more than needed – a costly mistake!

11.7.2 Setting Time

Dentists thrive on fast-setting products, but the original ProRoot MTA powders mixed with water required more than 2 h to set [37]. Newer bioactive ceramic cement products have shorter initial setting times, often about 15 min [56]. The final (effective) setting time for the non-resin products is longer, usually several hours. Various means have been used to reduce the setting time, including the use of finer particles and the inclusion of calcium chloride, reduced calcium sulfate content, and

water-soluble polymers in water-based solutions for mixing with powders. Higher temperature and humidity and smaller and thinner samples speed the setting of the bioactive ceramic cements.

Setting time for these cements has been measured with the Gilmore indentation apparatus. The Gilmore apparatus has two indenters: one indenter has a larger diameter and a lighter weight to judge the initial set time, and the other indenter is heavier, which has a smaller diameter indenter for the "effective" (final) set. Unset materials allow an indentation on the sample surface. Notably, the current initial and effective (final) setting times for the bioactive ceramic cements are longer than required for base or liner materials (less than 10 min) in ISO 9917-1 or ISO 3107 standards for water-setting cements and zinc-oxide eugenol materials.

A few bioactive ceramic cement products have compensated for longer setting times than "conventional" dental materials by being washout resistant. Completion of setting of the bioactive cement is not required for many indications, such as pulpotomies and crown placement. Some bioactive cement products easily remain within the pulp chamber; while a crown is seated, setting is completed after the procedure. Products with gels for mixing with the powder and the single cement pastes create excellent washout resistance. Bioactive cement powders that are mixed with plain water or anesthetic solution are not washout resistant. When a crown preparation is required after the pulpotomy, a thin layer of glass ionomer cement, compomer, resin-modified glass ionomer, or flowable composite can be used to stabilize the bioactive ceramics in the pulp chamber; these restorative materials enable easier rinsing after crown preparation is complete and stabilize the bioactive cement. Despite the perceived goal for fast-curing, the newer, washout-resistant products, including the slower-setting single pastes, are popular and convenient.

The products discussed above all rely on the hydration of the cement to set. Dentists are very familiar with fast-setting, light-curing, single-paste composites for restoratives, which start to set when exposed to blue light. Dual-paste products are also common in dentistry, where the components are mixed to start the setting reaction. Some two-component, resin-based materials are dual-cured, that is, light and chemical curing occurs. Resin-based products containing bioactive cements available from BISCO or NuSmile contain the calcium silicate cements but rely on the setting of their polymer (resin) matrix (Fig. 11.6e). TheraCal LC paste contains a light-curable resin as does NeoLiner LC. TheraCal PT is a two-paste, dual-cured, resin product for pulpotomies. Resin-based materials are also washout resistant, but not as clinically effective as non-resin-based cements because the resin matrix controls the release of ions from the bioactive powder.

11.7.3 Solubility

Bioactive calcium silicate/aluminate cements are classified as a permanently implanted material according to ISO 7405, a standard for biocompatibility of dental materials this is an indication where the material should be insoluble and, usually, non-porous. Researchers have reported some cement products have less than 10%

porosity, with one-half being closed pores, and solubility less than 3% after 72 h [57]. Others have reported high solubility (~20%), water sorption (~12%), and porosity (40%) for other products [58]. These solubility measurements are a point of confusion because high porosity or solubility would allow bacterial migration and dissolution, which is contrary to the excellent clinical performance of bioactive ceramic cement materials.

Calcium silicate and calcium aluminate bioactive cements inherently release calcium and hydroxide ions into the tissue and create a high pH (>10) environment, which continue to be released over 4 weeks in diminishing amounts. The chief benefit of the persistent alkalinity has been the formation of the biomineralization layer on the surface, but it also contributes to local antibacterial [59] and antifungal effects [60]. The solubility test method of the ISO 6876 standard tests requires that samples with a high surface-to-volume ratio be soaked in water then the material eluted into the solution is measured. This method emphasizes the weight loss from the dissolution of calcium hydroxide from the surface, but calcium hydroxide is essential for bioactive bioceramics. The test method currently does not measure the insolubility of the cement matrix. The test method is inappropriate for these cement materials and doesn't illustrate the stability of the calcium silicate and calcium aluminate cements. As a practical point, if calcium silicate cements were soluble, concrete structures would dissolve and collapse!

11.7.4 Dimensional Stability

Dental materials may shrink or expand during setting. Shrinkage can allow bacterial infiltration (microleakage), and expansion can cause tooth fracture. Microleakage avoidance is important in preventing bacteria in the oral cavity from migrating into the tooth or reaching the alveolar bone. Many test techniques have been used to assess leakage: dye penetration, dye sorption, bacterial or endotoxin infiltration, and fluid filtration. The lower microleakage of the bioactive ceramic cement products is well established, particularly compared to amalgam or zinc oxide-eugenol cement. Lower microleakage may be attributed to the dimensional stability [61, 62] of the bioactive ceramic cements. Linear changes as small as 0.5 to 1.0% [61] after 30 days have been measured, with some dependence on the powder-to-water ratio used for mixing. Volumetric changes have also been reported from computerized microtomography (μCT) tests; however, the results are less than ±1% [63]. This dimensional stability is another advantage of using these calcium cements.

11.7.5 Bonding

Bonding is essential for restorative materials, and shear bond strengths to tooth structure are expected to be high. The bioactive ceramic cements are placed under restorative materials, and they function to stop bacterial migration and induce pulpal or periapical tissue healing; they are not used for their adhesive qualities. Pushout

strength tests have been used to test calcium silicate materials' bonding to teeth. Such tests have also served as a surrogate for assessing microleakage, shear bond strength, and dentinal tubule penetration. The pushout bond-strength values vary widely, and the techniques have been criticized [64] for the experimental designs. Generally, any bonding values have been low compared to restorative materials.

Etching is a common procedural step for bonding in dentistry, but etching is of no benefit in placing restoratives over bioactive cements. Acids will soften, not roughen, the hydrated matrix of the calcium cements; neither chemical nor mechanical adhesion occurs via etching the bioactive ceramic cements. Nor have polymer adhesives over the calcium silicate/aluminate cements have improved bonding [65]. A high bond strength of these materials to restoratives or teeth is not essential, and high bond strengths have not been measured. The likelihood of displacement or "debonding" of the bioactive cements is very low because they are used intracoronally. No case reports of dislodgement of the calcium silicate cements have been published. Bonding restorative materials over the bioactive ceramic cement should focus on bonding the restorative to the surrounding tooth structure, without expecting any added benefit of bonding to the underlying bioactive cement.

11.7.6 Strength

Ceramic materials perform best in compression and are weak in tension. Luckily, for pediatric dental indications, the bioactive cements undergo compressive forces under a restorative material. Compressive strengths have varied widely for bioactive cements. Some materials meet the ISO 9917-1 standard's requirement (>50 MPa), with the caveat of testing after a few days of setting, not after the 24-h time period given in the test method [37]. However, in the ISO 3107 standard for zinc oxide eugenol used as a base, the requirement is only 5 MPa; therefore, bioactive ceramic cements can be used as a base, e.g., indirect pulp capping. An interesting aspect of the calcium silicate cements is that strengthening (hydration) continues after setting, for about 4 weeks [66], unlike other dental materials.

11.7.7 Costs

The cost of the original MTA products has been a sore point between manufacturers and dentists [16]. Costs are now lower than the original materials [27], although still significant on a per dose basis, compared to other dental materials. Competition among manufacturers is expected (hopefully!) to continue to lower the price per dose to levels competitive with other dental products. Today, multi-dose, powder-liquid systems are very economical per dose. The single-paste materials have minimal waste and may be affordable if judiciously dispensed.

11.7.8 Other "Bioactive" Materials

The bioactive ceramic cements have prompted a trend in dentistry for companies to advertise materials as "bioactive." Some nominally "bioactive" materials release ions, but do not create the surficial hydroxyapatite layer created by the calcium silicate and calcium aluminate cements. Clinical benefits of bioactivity may be absent or erroneously advertised in materials such as resin-modified glass ionomers that release ions; sometimes, the SEM/EDS spectra in teeth have been misinterpreted. Glass-ionomer cements are well known in dentistry for their fluoride ion release, which does exchange at body temperature into the apatite of enamel or dentin, to harden (remineralize) the tissue. However, fluoride ion release alone does not create biomineralization/bioactivity, that is, formation of HA. "Giomer" glass releases six ions that may be beneficial, but not form a HA layer: fluoride, sodium, strontium, aluminum, silicate, and borate. The pH created by glass ionomer cements is less than 7, which is unable to cause the biomineralization reaction of Eq. 11.1. The term "biointeractive" is more appropriate for such products, rather than bioactive or biomineralizing. No well-documented clinical and histological evidence bioactive ability has been published for biointeractive materials, and some analyses are spurious using SEM/EDS analysis.

11.8 Summary

Bioactive calcium silicate and calcium aluminate ceramic cements are wonderful materials for pediatric dentistry, general dentistry, and endodontics. Contemporary calcium silicate or calcium aluminate cement products are known by many names; chief among them is MTA, which is a trade name that indicates products containing the calcium silicate cement powder. The key to these bioactive calcium cements' performance is the bioactivity/biomineralization that occurs because of their high pH and calcium ion release when the cements react with water. The ion release continues over a few weeks, providing local antimicrobial effects. The products containing the bioactive bioceramic cements form a layer of hydroxyapatite in contact with tissue fluids. This layer assists with healing, unlike alternative treatments such as formocresol or ferric sulfate.

Bioactive bioceramic products have been improved over the past 25 years since their introduction. Newer products have finer powders and convenient liquids or gels that make handling and placement easier with stability when placed (washout resistance). Various additives have reduced the setting times of the powder/liquid products although the cement products set more slowly than composite materials. Powder-liquid products usually set in about 15 min, but do not delay a procedure; completion of setting is not required before a restorative is placed. Novel pastes have made the bioactive cements more convenient for pediatric dentists; they can be the most cost-effective and convenient and set in vivo over a few hours.

Discoloration has been eliminated, even for some products with the trade name "MTA," by choosing products without bismuth oxide. These bioactive cements have only limited ability to bond, but their high dimensional stability and insolubility is suitable for preventing microleakage. Packaging innovations have included unit-dose and multi-dose products, for convenience and economy. Products with resins for light-curing or dual-curing exist, but don't have the same bioactivity or versatility as the powder/liquid or self-setting paste products.

Bioactive cements eliminate the need for formocresol and its potential health risks. Furthermore, bioactive cements do not cause the internal resorption that has characterized ferric sulfate-treated pulpotomies. No significant differences have been confirmed among the non-resin products for histological performance; however, clinicians may choose a product based on convenience or cost. Resin-containing products remain confined to limited indications with fewer benefits than the other products.

With the continuing clinical success of such products, pediatric dentists should embrace these bioactive ceramic cements for their "everyday" dental procedures to offer the highest level of care. Bioactive cement products will continue to evolve for new indications, such as primary tooth pulpectomies, cervical resorption, and socket grafts. When all their physical properties are considered, calcium silicate and calcium aluminate cements are well suited as pediatric dental materials for procedures contacting pulp and periapical tissues. The clinical results, discussed in other chapters, confirm that the bioactive bioceramic cements are the new gold standard for minimally invasive, conservative pediatric dentistry procedures.

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Primary and Permanent Teeth Treated with Direct Pulp Capping

12

James A. Coll

Contents

12.1 Purpose

Direct pulp cap (for primary teeth occurring during caries removal) has been advocated by the American Academy of Pediatric Dentistry (*AAPD*) since 2017 [1, 2]. DPC has been shown to be an effective treatment after carious exposures in permanent teeth for a longer time [3, 4]. For permanent teeth, the American Association of Endodontists (*AAE*), in 2013 and updated in 2019, advocated DPC only for

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mechanical exposures during caries excavation [5]. More recently, the AAE issued a new position paper on vital pulp therapy (*VPT*) [6]. It stated calcium silicate-type materials such as MTA should be used for VPT. For asymptomatic or symptomatic permanent teeth with irreversible pulpitis, DPC success has been reported after 1 year as 94.7% [7] and after 2–3 years 84–86% in cariously exposed vital molars [8].

12.2 Goals

The goals of this chapter are to provide the reader with the most current evidence-based research on primary and permanent teeth DPC success.

12.3 Definitions

Bioceramics refers to any of the calcium silicate pulp materials for DPC or pulpotomy.

MTA stands for mineral trioxide aggregate which is a mixture of calcium silicate cements (primarily tricalcium and dicalcium silicate), bismuth oxide, and smaller amounts of dicalcium silicate, tricalcium silicate, tetracalcium, aluminoferrite, and calcium sulfate dihydrate known as gypsum.

Primary teeth DPC is indicated for carious pinpoint to 1 mm pulp exposures [2].

Permanent teeth DPC indicated for 0.25–2.5 mm pulp exposures resulting from caries removal [9].

Primary tooth reversible pulpitis is the pulpal diagnosis for a tooth without signs or symptoms of irreversible pulpitis that has provoked pain from eating for a short duration (5–10 min) [10].

Primary tooth irreversible pulpitis and/or necrosis will exhibit any one of the following: history of unprovoked toothache; sinus tract, soft tissue pathology, or gingival swelling not associated with periodontal disease; abnormal mobility not associated with exfoliation; radiographic furcation or periapical radiolucency; external or internal radiographic root resorption [10].

Definitions by the AAE are as follows: [11]

Permanent tooth, reversible pulpitis is based on subjective and objective findings indicating that the inflammation should resolve and the pulp return to normal. **Permanent tooth asymptomatic irreversible pulpitis** is based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing due to inflammation produced by caries, caries excavation, or trauma but is asymptomatic.

Permanent tooth symptomatic irreversible pulpitis is based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing and has lingering thermal pain, spontaneous pain, or referred pain.

12.4 Pulpal Diagnosis

For pulpal diagnosis in primary and permanent teeth, see Chap. 9. However, it is known diagnostic tests are of limited value in primary teeth and in immature permanent teeth [12]. There is insufficient EBD research to make a recommendation to accurately diagnose the pulp's vitality resulting from deep caries in primary teeth. The best assessments are from symptoms, palpation, percussion, and tooth mobility. For immature permanent teeth, the same assessments apply; for permanent teeth with mature apexes, cold, heat, percussion, and electric pulp tests can aid the diagnosis.

12.5 Caries Removal Methods Affect Pulpal Treatment Methods

12.5.1 Complete Caries Removal

Complete caries removal has also been termed "non-selective" whereby all caries is removed till hard dentin is reached [13]. This method involves removing all the infected and affected carious dentin with burs, hand instruments, or chemical methods.

12.5.1.1 Complete Caries Removal and Rate of Pulp Exposure

A pulp exposure can occur when complete excavation of deep caries is employed.

A meta-analysis showed for deep caries in primary and permanent teeth complete caries excavation has three times the odds ratio of creating a pulp exposure compared to selective or stepwise excavation [14]. Another systematic review [15] showed partial caries removal reduced the incidence of an exposure by 77% compared to complete excavation. In 2016 a meta-analysis showed almost half the dentists in practice still employ complete caries removal for deep caries in primary and permanent teeth [16]. As a result of these studies and other reasons, complete caries removal for deep caries is not recommended [17].

12.5.2 Stepwise Caries Removal (SW)

An alternative method of deep caries removal is stepwise caries removal. It is accomplished over two patient visits. The first visit completely removes the decayed dentin along the peripheral walls till hard dentin is reached. On the pulpal floor, caries is removed till soft dentin is reached avoiding a pulp exposure [13]. A temporary restoration such as a glass ionomer is placed covering the soft dentin on the pulpal floor (Figs. 12.1 and 12.2). The theory is that SW will allow remineralization of the

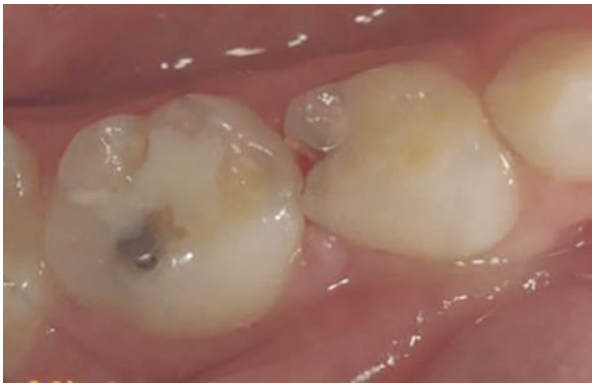


Fig. 12.1 Preoperative view of interproximal caries in first primary molar before stepwise caries removal

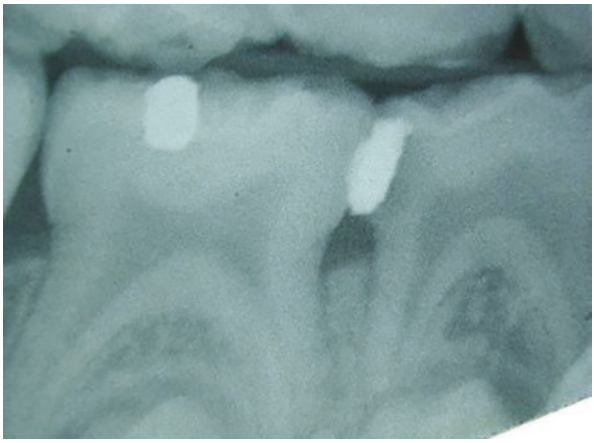


Fig. 12.2 View of first primary molar and temporary filling after first visit of stepwise caries removal

affected dentin and form more tertiary dentin [18]. The carious lesion is reentered in 8–12 weeks and caries removal carried out leaving only central yellowish or grayish hard dentin in the pulpal floor (Fig. 12.3). A final restoration is placed with the intention to seal the pulp from any microleakage [19]. Systematic reviews and meta-analyses have shown SW significantly reduced pulp exposures compared to complete caries removal [14, 15].

12.5.3 Selective (Partial) Caries Excavation

The third type of caries excavation is termed "selective or partial caries removal." It is completed in one appointment where the dentist completely removes the peripheral decay but intentionally leaves the deepest leathery caries in place and covers it with a well-sealed durable restoration [13]. Selective caries removal done in one appointment with local anesthesia would be the recommended treatment for children. This method is used for indirect pulp treatment and normally avoids a pulp

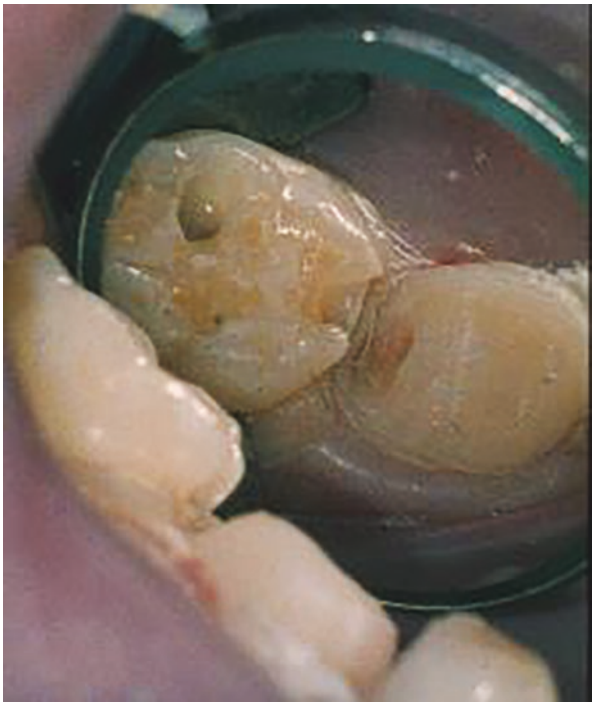


Fig. 12.3 Second visit stepwise excavation showing central yellowish hard dentin after second caries removal visit

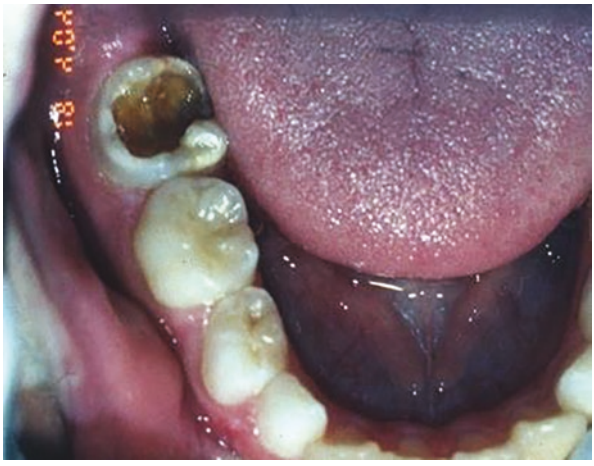


Fig. 12.4 Preoperative view before selective caries removal in a mandibular permanent right first molar

exposure (Figs. 12.4 and 12.5). Selective caries removal omits the reentry and second excavation done with SW and avoids having to administer anesthesia a second time (Fig. 12.6). In addition, possible failure of a temporary filling done with SW is avoided. Selective removal tries to shift the microbial balance in deep lesions to allow dentin remineralization and arrest the carious lesion.

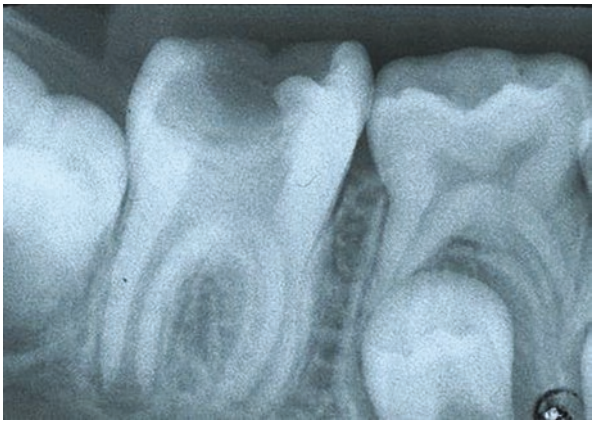


Fig. 12.5 Radiographic view before selective caries removal mandibular permanent right first molar

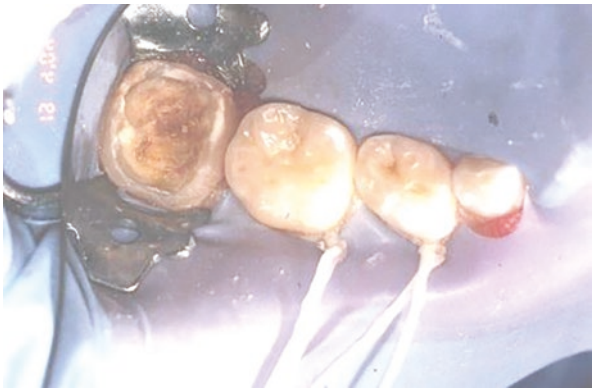


Fig. 12.6 View after selective caries removal leaving the deepest caries in place in the mandibular permanent right first molar

Maltz et al. [20] published the results of a randomized controlled trial (**RCT**) where SW and selective caries removal were compared in 299 permanent molars.

The results of the 3-year follow-up showed a significantly higher success rate of 91% for selective removal compared to SW success of 61%.

Maltz et al. speculated on reasons why stepwise excavation success was only 61% after 3 years. It was noted that some SW patients did not return for the second appointment at the correct time, and the success rate in these patients was only 13%. Patients treated with SW that had a final excavation and permanent restoration in 1–2 months had success rates not statistically different from selective removal of caries (88% SW vs. 91% selective removal).

12.5.4 No Caries Removal

Another type of caries management has been reported only in primary teeth. It involves no caries removal and placement of a steel crown to seal the caries and stop the carious process. The technique is termed the Hall technique [21, 22]. The 48-month results [22] showed significantly better success ($p = 0.0005$) using the

Hall technique versus complete caries removal and a filling which was usually glass ionomer.

12.6 Vital Pulp Therapy for Carious Pulp Exposure Having Normal Pulp or Reversible Pulpitis Diagnosis

12.6.1 Direct Pulp Capping Primary Teeth

Direct pulp capping is ideally done for primary teeth diagnosed as having a normal pulp. The AAPD 2020 Guideline has a Decision Tree figure showing DPC also indicated for reversible pulpitis [10]. The caries excavation causes an exposure normally as a result of using complete caries removal for deep caries. The DPC capping material is placed on the exposure in an effort to maintain the pulp's vitality. It is theorized the DPC will enable the pulp to form tertiary dentin at the exposure site to form a dentin bridge [23]. DPC procedures in vital primary teeth are indicated for pinpoint to 1 mm sized mechanical or carious exposures [2]. DPC is contraindicated in teeth with irreversible pulpitis. The clinical procedure should be done under rubber dam isolation using local anesthesia. The clinical caries is removed using high and low speed burs and/or hand excavators revealing an exposure (Fig. 12.7). When an exposure is encountered, the area is preferably rinsed for a DPC with an antimicrobial such as sodium hypochlorite (NaOCl) (1–5%) (Fig. 12.8). Then a moistened cotton pellet with NaOCL is pressed on the pulp exposure for 1–2 min. After

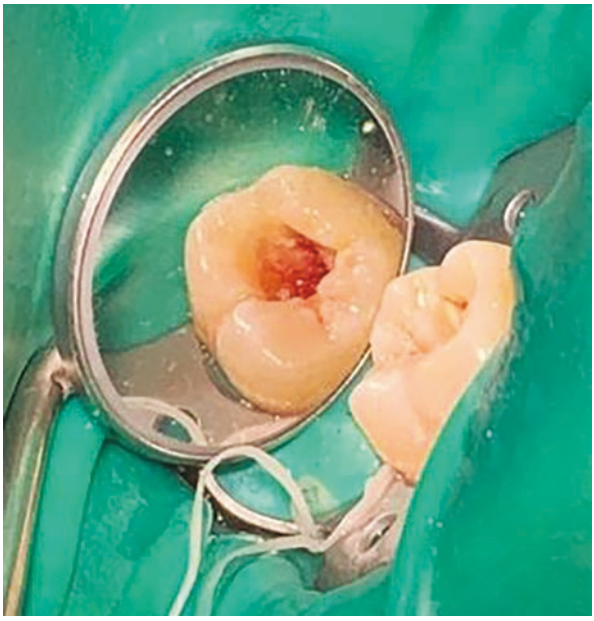


Fig. 12.7 Carious exposure after complete caries removal

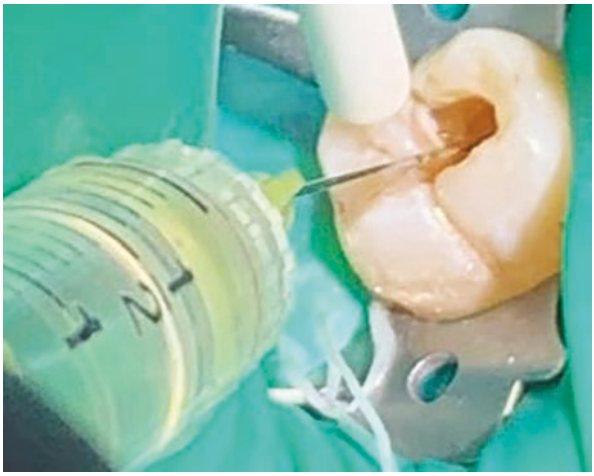


Fig. 12.8 Sodium hypochlorite used to rinse exposure site

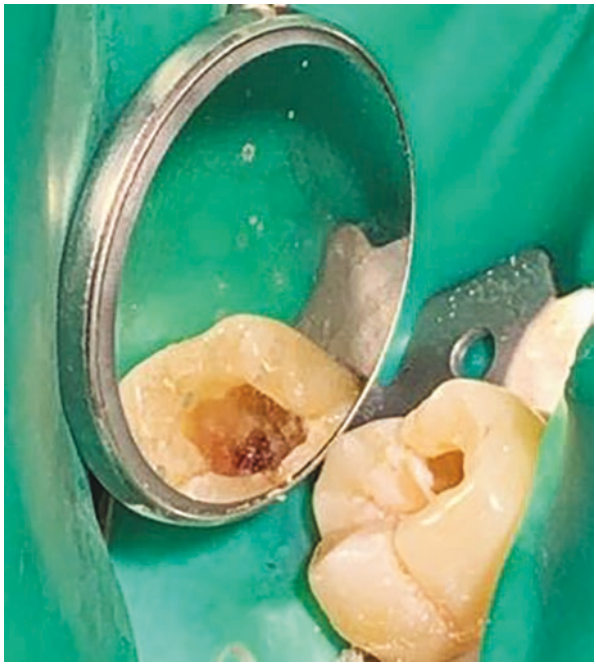


Fig. 12.9 Exposure after hemorrhage is controlled

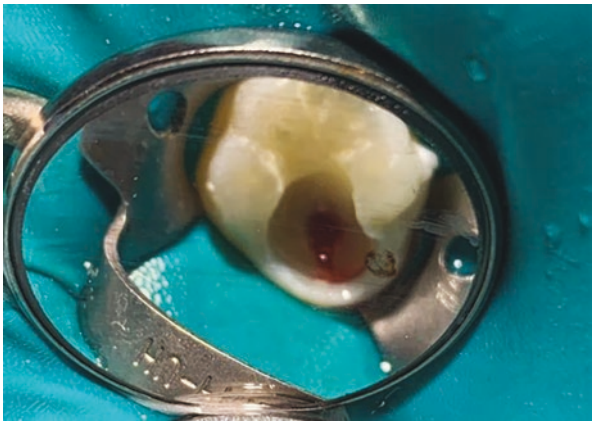
hemostasis is obtained, the area is rinsed with saline or water and blotted with dry cotton pellets to remove the excess saline (Fig. 12.9).

A 2 mm MTA or another bioceramic material is placed over the exposure with a plastic instrument or amalgam carrier. Calcium hydroxide paste can also be used as an alternative and was not significantly different in success from alternate capping agents [1]. If MTA is used, cover it with a resin-modified glass ionomer or a self-setting glass ionomer before the final restoration.

The EBD research has shown success of DPC in primary teeth was reported as 88.8% after 24 months [1]. This was based on the combined clinical and radiographic overall success. This evidence at 24 months [1] showed the capping agent had no significant difference on DPC success. It must be noted that two of the three 24-month studies only included teeth with occlusal caries [1]. In addition, two studies tested DPC versus indirect pulp cap (IPT) with 12-month results. One study [24] was a prospective non-randomized design and the other [25] a retrospective design. Their pooled successes after 12 months were IPT 96% (218/226) and DPC 70% (14/20). There are three studies comparing DPC using MTA to alternative capping agents. The results for 12 months showed MTA success at 92% (93/101) and alternate capping agents 89% (89/100) with RR 1.02 (0.95, 1.09) $p = 0.67$. The alternate agents were other bioceramic materials or calcium hydroxide.

12.6.2 Direct Pulp Capping Permanent Teeth

DPC in permanent teeth is one method of performing VPT. Bjorndal [19] reported carious exposures treated with CH for the DPC had success after 1 year of only 31.8%. A systematic review found carious exposures treated with DPC using CH and MTA had a success rate of 72.9% for teeth followed 3 years or more [3]. A more recent EBD systematic review and meta-analysis found treating a carious exposure with DPC was significantly more successful using MTA and Biodentine compared to calcium hydroxide (**CH**) [8]. All the included teeth had mature apexes. They reported DPC using MTA compared to CH after 2- to 3-year follow-up was significantly superior (OR 2.21, 95% CI; 1.42–3.44, $P = 0.0004$). MTA success after 2–3 years was 84% and Biodentine 86%. The pulpal diagnosis of the included teeth was either normal or reversible pulpitis. Therefore, permanent tooth DPC is indicated for mechanical and carious permanent tooth pulp exposures with immature or mature apexes having normal or reversible pulpitis.



Figs. 12.10 Carious exposure before hemorrhage controlled

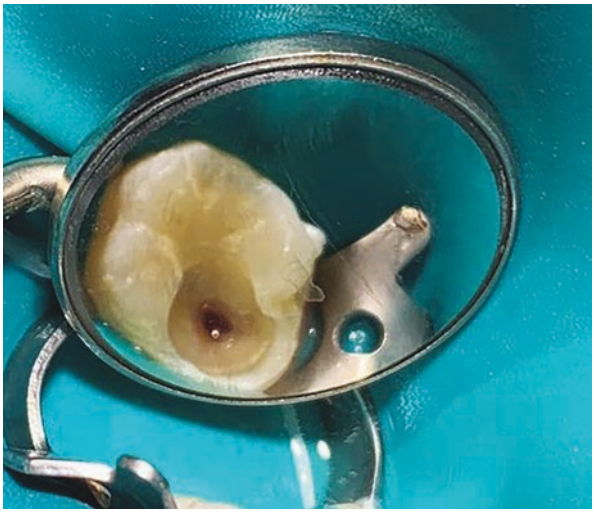


Fig. 12.11 Carious exposure after hemorrhage controlled

The method of DPC is similar to that for primary teeth. The treatment should be under a rubber dam using local anesthesia. The carious tissue is removed usually employing complete caries removal so that a pulp exposure occurs. It may be a mechanical or carious exposure (Fig. 12.10). The exposure size of less than 2.5 mm can be enlarged so it can be rinsed with NaOCL (5.25–6%) [9]. Then a cotton pellet soaked in NaOCl is used to apply pressure and stop the hemorrhage in less than 6 min [9]. Rinse the area with saline or water and blot dry the exposure site (Fig. 12.11). Apply MTA or Biodentine or another calcium silicate-based material to a thickness of 2–3 mm with a plastic instrument or amalgam carrier. Compact the material with a cotton pellet slightly moistened with water. Cover the material with a self-setting glass ionomer or resin-modified glass ionomer. Then restore the tooth with a well-sealed restoration.

12.7 Vital Pulp Therapy for Carious Pulp Exposure Having Irreversible Pulpitis Diagnosis

A 1-year RCT evaluated four VPT's using CEM which is a biceramic material for IPC, DPC, and partial and full pulpotomy [7]. All teeth had a mature apex and caries in close proximity to the pulp. There were 26% of the 73 DPC teeth diagnosed with irreversible pulpitis, and all but one had a carious pulp exposure. After 1 year, the data showed DPC clinical and radiographic combined success was 94.7%. An RCT in 6–18-year-old children with permanent teeth had caries ¾ into the dentin [26]. Some teeth had a clinical diagnosis of irreversible pulpitis, and all were treated with DPC using either with MTA or Biodentine. The successes after 18 +/- months were 92.6% for MTA and 96.4% for Biodentine ($P > 0.05$). The failures were not the teeth with periapical involvement. The AAE 2021 position paper on vital pulp

therapy challenged the pulpal diagnosis of teeth that can receive VPT [6]. This paper cited a study suggesting there is no actual histologic boundary showing a vital pulp is beyond repair [27]. This would mean a permanent tooth DPC and pulpotomy could be indicated if it is diagnosed with irreversible pulpitis, either symptomatic or asymptomatic. The position paper went further by recommending unroofing the pulp so direct observation of the pulp with a surgical microscope will allow the final diagnosis. There is no study showing direct visualization of vital pulps allows for a better pulpal diagnosis for a permanent tooth with deep caries.

12.8 Considerations Before DPC in Primary and Permanent Teeth

MTA has the potential to cause a gray discoloration while Biodentine and CEM are reported to cause minimal or no discoloration [7, 26]. Valles [28] reported significant color changes in white MTA Angelus and ProRoot MTA due to the bismuth oxide in the materials. The reason for the discoloration may be the interaction of the bismuth oxide with NaOCl or blood. In this study, Biodentine exhibited color stability for 5 days. Teeth in need of esthetic restorations such as a composite, Biodentine or another bioceramic restoration, that does not discolor, would be recommended.

The setting time of the bioceramic materials differ and are of clinical importance. Biodentine has a shorter final setting time (about 10 min) compared to ProRoot MTA of almost 3 h [29]. There is a setting accelerator added to Biodentine that speeds up the setting time. MTA's slower setting time makes its manipulation more difficult for some compared to Biodentine and other faster setting bioceramic materials. When using MTA for DPC, it's best to cover it with a self-setting glass ionomer or resin-modified glass ionomer.

In primary teeth, there was no significant difference in DPC 24-month success reported between MTA and other alternative capping agents and CH [1]. For permanent teeth and primary teeth intended to be retained longer than 24-months, MTA is likely the better choice. Lin [30] reported bioceramic materials released more calcium and were consistent in raising the pH levels more than calcium hydroxide materials like Dycal. This article speculated increasing the alkalinity promotes release of TGF-beta1 from the dentin and promotes reparative dentin formation. In addition, the calcium hydroxide DPC materials like Dycal are more water soluble after 90 days and likely diminish its sealing ability [30].

Use of lasers for DPC is still being investigated. In primary teeth, clinical RCT studies using laser DPC versus other DPC treatments have not been published. In permanent teeth, there are EBD studies showing shorter-term DPC success with laser of 92% (24/25) at 12 months [31] and laser-assisted DPC (100% success [32]) where the capping agent may be MTA but a laser was used prior to placing the DPC agent. At this time, DPC using a laser would need to be at the clinical expertise of the practitioner after consulting with the patient.

The younger aged patient may be an advantage when doing DPC on permanent teeth (Fig. 12.12). A retrospective study [33] with a mean follow-up of over 6 years

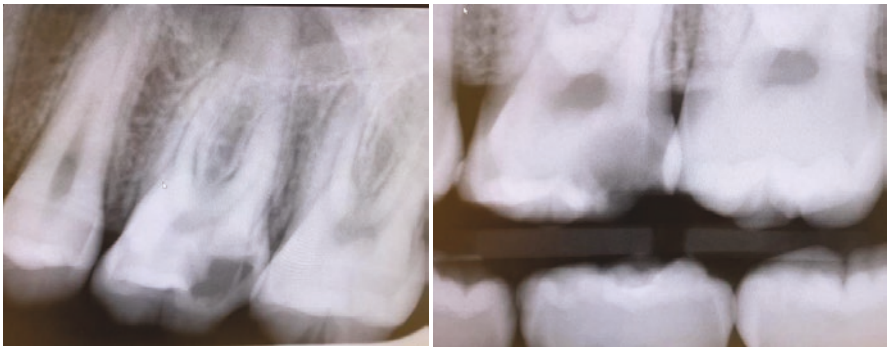


Fig. 12.12 Preoperative images maxillary left first permanent molar with preoperative pain in a 12-year-old male

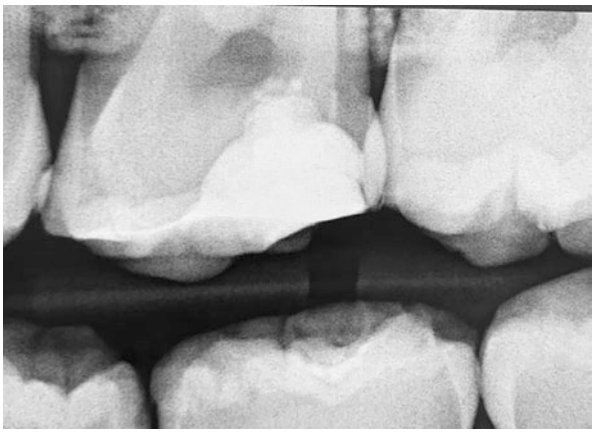


Fig. 12.13 Postoperative image of #14 with MTA DPC and composite resin restoration

found younger aged patients (16–20 years old) had the highest rate of DPC favorable treatment using calcium hydroxide (Figure 12.13). The study also found after 6 years, out of 49/199 having unfavorable outcomes, 39/49 (80%) had spontaneous pain preoperatively.

12.9 Conclusions

- Direct pulp capping in primary teeth is indicated for carious exposures less than 1 mm in size. MTA has a DPC expected success rate of 88% after 24 months in primary teeth.
- In permanent teeth, direct pulp capping is indicated for carious exposures less than 2.5 mm when the tooth has no signs or symptoms of irreversible pulpitis.
- Permanent tooth DPC in teeth with irreversible pulpitis has shown 12–18-month success but longer-term RCT studies are not available.

- Permanent tooth carious pulp exposures treated with DPC using MTA or Biodentine have an expected success rate of 84–86% after 2–3 years and are significantly better than using calcium hydroxide.
- Permanent tooth DPC is indicated for teeth with either immature or mature apexes.

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Pulpotomy for Primary Teeth: Techniques and Materials

13

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13.1 Introduction

In the previous chapters, we have reviewed the importance and benefits of the contemporary trends of conservation of form and function, in the case of vital pulp therapy, through the preservation of primary tooth vitality. The advantages of preserving a tooth in the arch until natural exfoliation followed by immediate replacement by a succedaneous tooth are important at all levels: for control of local symptoms and restoring function (tooth level), arch spacing (mouth level), for the child's well-being (individual level), and for reducing the need for further treatment, either space maintenance or space management with all the costs they incur (community level). Minimally invasive approaches, including "selective caries removal to soft dentin" (indirect pulp treatment) and direct pulp capping, have been discussed earlier in this book. In this chapter, we will go one step further discussing pulpotomy as an alternative treatment for vital primary teeth with deep caries.

Pulpotomy is a vital pulp therapy procedure that aims to remove the inflamed/infected tissue in the coronal pulp chamber and place a medicament that will aid to restore health and preserve the vitality of the remaining healthy portion of the radicular pulp. The pulpotomy procedure is indicated when caries removal results in pulp exposure in a primary tooth with a normal pulp or reversible pulpitis or after a traumatic pulp exposure, and when there are no radiographic signs of infection or pathologic resorption [1]. It has been an effective and widely accepted procedure for the treatment of teeth with deep caries or trauma for decades.

The efficacy of pulpotomy varies with the materials used, and historically, there has been a quest for the perfect medicament and/or technique. An ideal pulpotomy material should control the existing bacterial infection while being biocompatible with the remaining tissues, capable of inducing hard tissue formation while not affecting physiologic root resorption, in addition to being affordable. Buckley's formocresol was introduced for this purpose in the early 1900s [2]. The use of a pulpotomy technique was described in 1930 [3] becoming the preferred technique and gold standard for decades. Because of its limitations and concerns for toxicity [4], other materials and techniques have been tested and used over the years (Fig. 13.1 timeline).

These materials are used with different aims as they have different mechanisms of action on the remaining pulpal tissue. Some of them contain fixing agents (formocresol and glutaraldehyde), others are hemostatic (ferric sulfate), others are antibacterial (sodium hypochlorite (NaOCl)), others contain corticosteroids as anti-inflammatories and antibiotics for bacterial control (Ledermix), and some like zinc oxide and eugenol (ZOE) were used because of the historical use of eugenol as a desensitizer. Non-pharmacotherapeutic approaches like electrosurgery and lasers, aim to cauterize the surface of the remaining radicular pulp tissue to eliminate the residual infection. Regenerative materials aim at forming a calcium bridge and inducing reparative dentin. The earliest example of this class, calcium hydroxide $(CaOH)_2$, had limited success as its increased alkalinity causes inflammation and necrosis, leading to internal resorption. More recent regenerative, bioactive calcium silicate cements like mineral trioxide aggregate (MTA), and Biodentine have

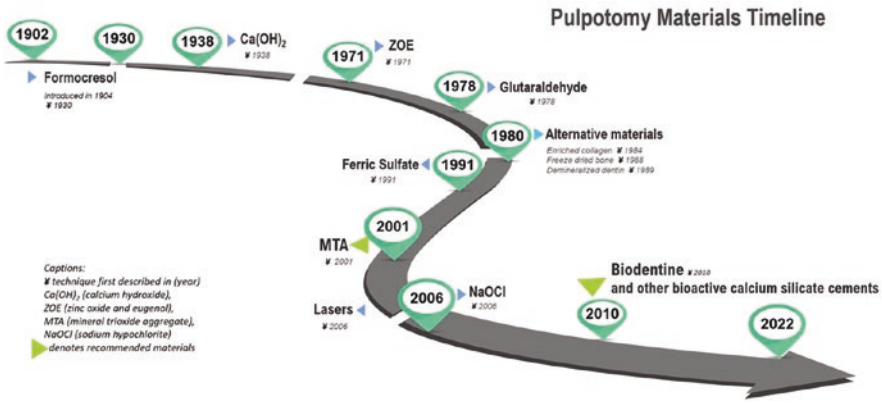

Fig. 13.1 Pulpotomy materials timeline

stepped up to be not only comparable to the gold standard, but preferable for many different reasons.

Some of these materials and techniques never gained popularity as they did not perform clinically as well as formocresol and/or produced undesirable effects like pulp inflammation, pain, and internal resorption. Some other materials continue to be used by clinicians despite their limitations, whether it be their lower efficacy or their undesirable side effects. This chapter does not include descriptions of materials and techniques no longer used like Ledermix and electrosurgery, but we will discuss the advantages and limitations of the most widely used materials and techniques, including their success rates, considering the results of several recent systematic reviews which have combined the data of numerous clinical trials performed in many different countries. Their results include direct or indirect comparisons between materials that help establish evidence-based recommendations for clinicians to have the best chances of success when performing a pulpotomy to manage primary teeth with deep caries or trauma. It is important that we discuss all of them in context because although technology continues to develop and with the emergence of new bioactive calcium-silicate cements, current comparative studies have not yielded enough high-quality evidence to make solid recommendations for a single gold standard material for pulpotomies on primary teeth.

13.1.1 Formocresol

The formula proposed by Buckley that uses 19% formaldehyde, 35% cresol, and 15% glycerin in distilled water [2] is known as formocresol. Formaldehyde is a fixative agent that is bactericidal and inhibits enzymes in the inflammatory process. Its use as a pulpotomy medicament was described in 1930 [3], and the original aim of using formocresol was to completely fixate all the residual pulp tissue and necrotic material within the root canal. Recommended initial techniques included a two-visit

treatment where a cotton pellet with full-strength formocresol was left on site in between appointments, and a one-visit treatment where the cotton pellet with formocresol was placed on the pulpotomy site for only 5 min. Formocresol was applied after removing the coronal portion of the pulp and achieving hemostasis, and after its application the pulp chamber was filled with ZOE, and final restoration was placed. Histologic findings on these techniques highlight its cytotoxicity, which ranges from slight inflammation to total degeneration and necrotic changes of the remaining pulp tissue [5]. As a result, internal resorption and periapical and furcation radiolucencies were often found on treated teeth [6].

In an attempt to reduce the cytotoxicity of full-strength formocresol, later studies found that using a one-fifth dilution was still effective and led to better clinical results [7]. Current techniques support limiting both dose and contact time as they aim to create only a superficial layer of fixation while preserving the vitality of the deeper radicular pulp. In addition to using a one-fifth dilution, the cotton pellet is pressed into a cotton roll before application to remove excess and limit the amount placed on the surface of the remaining pulp stump.

Historically, studies using formocresol as a pulpotomy agent report success rates ranging from 55% to 95% depending on the application protocol, the study design, the parameters for defining the success of the treatment, and the length of follow-up. A recent umbrella review of nine systematic reviews reports a formocresol mean clinical success rate of 99% and the radiographic success of 85% over a 24-month period [8]. These figures include the results of a systematic review comparing medicaments that reported that MTA pulpotomy was superior to formocresol. Compared with formocresol, MTA reduced both clinical and radiological failures, with a statistically significant difference at 24 months for radiological failure. Another recent systematic review [10] found that compared to formocresol, Biodentine had significantly lower clinical and radiographic failures over a period of 12 months.

These new results are very important because the potential systemic toxicity of formocresol has been a concern over the years. Cresol is locally destructive to vital tissues but presents negligible potential for systemic distribution following the pulp treatment technique. However, formaldehyde is distributed systemically after the pulp treatment technique, so its potential systemic toxicity has been a topic of debate for decades [11]. The fact that it is classified by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) as a known human carcinogen (IARC 2017) has resulted in its decreased popularity worldwide. Despite all this, its high clinical efficacy, affordability, and availability have kept it in use in certain areas, as until recently, no other materials had proven to be equal or better. This may be changing currently with the advent of more affordable biocompatible materials that will be discussed in this chapter.

13.1.2 Glutaraldehyde

Glutaraldehyde is a dialdehyde that was proposed as an alternative fixative to formocresol because of its potential lower toxicity and better tissue fixative properties,

despite the disadvantage of having a very short shelf life. Clinical studies using 2% glutaraldehyde applied for 1–5 min showed clinical success ranging from 90% over 18 months [12] to 88% over 24 months [13].

Its cytotoxicity was reported to be similar to formocresol, and a large number of treated teeth presented with internal resorption. With less clinical success than formocresol and questionable improved safety, studies have not justified recommending 2% glutaraldehyde to substitute for formocresol [13].

13.1.3 Calcium Hydroxide

Calcium hydroxide ($Ca(OH)_2$) has been in use since the 1930s and was proposed as a pulpotomy medicament because of its potential to induce reparative dentin and pulp healing [14]. However, studies have shown lower rates of success for calcium hydroxide pulpotomies since it was first used, ranging from 31% to 90% [15–17]. This variation could be due to the inclusion criteria for the studies, the wide variation of preparations used, and the follow-up time. Most failures are due to chronic inflammation that led to clinical and radiographic failures. The main drawbacks of $Ca(OH)_2$ are associated with its physical properties, as this non-setting material will go through degradation and dissolution over time, leading to infection and/or internal resorption. A more detailed description of calcium hydroxide can be found in Chap. 17. In recent systematic reviews comprising many prospective clinical studies, calcium hydroxide pulpotomies are reported to have a clinical success rate of 46% [8], which is significantly less successful than formocresol, ferric sulfate, and MTA, resulting in the recommendation against the use of calcium hydroxide as a pulpotomy medicament [9, 18, 19]

13.1.4 Sodium Hypochlorite

Sodium hypochlorite has been utilized as an irrigant during endodontic treatment due to its antibacterial properties while causing minimal pulpal inflammation in the remaining tissue [20]. For this reason, its use at 3–5% concentrations placed in the pulp chamber on a cotton pellet for 30 s was tested in several clinical studies, showing success rates comparable to ferric sulfate and formocresol at 12-month follow-ups [21]. However, available clinical studies with 18 and 24 months of follow-up show lower success rates than those of formocresol pulpotomies [19, 22]. With current better alternatives that offer better clinical and radiographic success, the use of sodium hypochlorite as an isolated medicament for pulpotomy has fallen into disuse.

13.1.5 Zinc Oxide/Eugenol (ZOE)

In search of non-aldehyde pulp therapy alternatives, several retrospective studies have reported using ZOE as a stand-alone medicament for pulpotomy with clinical

success rates comparable to formocresol when placing it after achieving hemostasis and immediately followed by a stainless steel crown (SSC) restoration [23, 24]. Historically it has been one of the most frequently used materials in dentistry due to its sedative and palliative properties in cases of pulpal pain [25]. However, diverse toxic effects have been reported when it is directly applied over the pulp since eugenol induces a chronic inflammatory response and inhibits the immune reaction of pulp defense [26] and increases the risk of internal resorption. Clinical studies report internal resorption in approximately 27% of teeth followed up at 24 months [27]. Retrospective studies show clinical success rates of over 90% at different time periods [28, 29]. However, more recent prospective studies with clinical and radiographic data show a success rate of 65% over a 24 month period, which is significantly lower than most other available pulpotomy materials, therefore making it unsuitable as a medicament of choice [19].

13.1.6 Ferric Sulfate

Ferric sulfate (FS) is a hemostatic agent that has traditionally been used for bleeding control. Its use was promoted as a pulpotomy agent to induce quick hemostasis and prevent clot formation, therefore improving the performance of whatever material was placed in the pulp chamber after it. Clinical studies using a 15.5–16% concentration have reported success rates similar to formocresol [30–33], with many of the reported failures being a result of internal resorption, leading to early exfoliation. The internal resorption has been attributed to the interaction of ferric ions and free release of eugenol from the ZOE used to cover the pulp stumps after hemostatic control with FS [34] as ZOE placed directly over the pulp tissue is reported to cause chronic inflammation that increases the risk of internal resorption [27]. A recent umbrella review of nine systematic reviews reports the efficacy of ferric sulfate ranging from 70 to 100% with clinical success always being higher than radiographic success at 24 months [8]. Success rates decrease at longer follow-up periods: one study reported 62% success at 36 months [35], and systematic reviews in the past have reported the superiority of MTA over FS [36, 37]. Although a recent systematic review [34] concludes that the clinical and radiographic outcomes of MTA and FS were not different at 24-month observation periods, they included studies with a high risk of bias, and their forest plots favor MTA over FS for radiographic success without reaching statistical significance. When including only low risk of bias prospective studies comparing ferric sulfate to currently available biocompatible materials, a more recent systematic review [19] reported the success of MTA being significantly higher than that of ferric sulfate at 24-month follow-ups. They report a clinically significant NNT (number needed to treat) of 5, which means that after doing five MTA pulpotomies, a dentist would prevent one failure if FS had been used.

Ferric sulfate continues to be used as it presents comparable clinical success to formocresol, but with fewer concerns about toxicity. With MTA and other biocompatible materials showing better performance over longer follow-up periods with

fewer radiographic signs of potential failures, they may present as a better option depending on the specific clinical situation.

13.1.7 Lasers

The use of lasers for pulpotomy was introduced as this technique could bypass the toxicity [38] and secondary effects of chemotherapeutic agents, with benefits including bleeding control and sterilization, to eliminate residual infection processes that would improve pulp cell healing promotion [39]. Several different lasers have been used in pulpotomy procedures in primary teeth including CO_2, Nd:YAG, InGaAIP, Er:YAG, and diode lasers, with the latter one being the most commonly reported laser for pulp therapy in children [40]. The clinical and radiographic success of laser pulpotomies ranges from 90% at 12 months to 93% at 24 months [41]. A systematic review on lasers reports that the laser technique shows comparable clinical and radiographic results to other conventional pulpotomy medicaments including formocresol and MTA after 18 months [40]. However, studies are typically small and with limited follow-up periods to make accurate comparisons [19]. More studies are required to confirm if and what kind of laser therapy can be an acceptable choice for a chemical-free option for a successful pulpotomy. Laser wavelength and other characteristics will need to be carefully defined.

13.1.8 MTA and Biodentine

The introduction of new bio-inductive and regenerative dental materials has improved the likelihood of finding better medicaments for pulp therapy as has been described in Chap. 11. The earliest material, mineral trioxide aggregate's (ProRoot MTA, Dentsply) main components include tricalcium silicate, dicalcium silicate, bismuth oxide, tricalcium aluminate, calcium sulfate dihydrate (gypsum), and calcium aluminoferrite, and their combination produces a colloidal gel that solidifies into a hard cement that induces the formation of dentin, cement, and bone [42]. Bismuth oxide is added for radiopacity, and calcium compounds react with the humid environment, releasing calcium hydroxide at decreasing rates over time. This results in a high pH of 12.5 that is inhospitable for bacterial growth and results in a prolonged antibacterial effect. Unlike calcium hydroxide products, it sets completely in the presence of moisture and has very low solubility, maintaining a hard, excellent marginal seal. It produces significantly effective dentinal bridging in a shorter time period with significantly lesser inflammation and pulpal necrosis than earlier similar regenerative materials like calcium hydroxide. MTA has been widely recognized as a superior material for vital pulp therapy because of its biocompatibility, good sealing properties, antimicrobial activity, and ability to set in the presence of moisture and blood. Its main drawbacks are its handling characteristics (long setting time of 3–4 h), discoloration of surrounding tissues, low radiopacity, incompatibility with other dental materials when layered, and higher cost [42]. Its success

rates as a pulpotomy agent have been described in numerous studies showing superiority over most other materials [9, 19, 43]

White MTA was developed to overcome the discoloration caused by the original ProRoot MTA, while showing comparable biocompatibility and success rates [44]. To overcome other disadvantages of original MTA, less expensive alternative bioceramic materials such as MTA Angelus (Angelus, Londrina, Brazil) with setting time of 10–15 min, MedCem-MTA Portland Cement (MedCem GmbH, Weinfelden, Switzerland) with zirconium oxide added as radiopacifier, and many others have been developed. Prospective studies of these products show no significant difference between clinical and radiographic outcomes when compared to the original compound [44, 45]. Another alternative calcium-silicate material, Biodentine (Septodont, Saint Maur-des-Fosses, France), has also been well studied in clinical trials. It is composed of tricalcium silicate cement, zirconium oxide, and calcium carbonate. With good biocompatibility and bioactive behavior, it stimulates [46] reparative dentin and dentin bridge formation, anchoring the material micromechanical to the underlying dentin. It is presented in a capsule with easy handling that sets in approximately 12 min and does not cause tooth discoloration. Its main drawback is poor bonding to the overlying resin restoration. Biodentine has shown higher success rates than formocresol [10, 47] and similar success rates to MTA in clinical trials [48–50]. Other new bioactive materials with different compositions aim to have better handling capabilities, compatibility to overlaying materials, minimal staining, and low cost [42]. Some of these materials, including NeoMTA2 and NeoPUTTY (Nusmile, Houston, TX, USA) which provide easy handling and low waste, TheraCal LC (Bisco, Schaumburg, Ill, USA) a light-cured resin-modified tricalcium silicate [51], and CEM cement (CEM, BioniqueDent, Tehran, Iran) a calcium-enriched mixture [52], and many others, are favored by clinicians around the world for their ease of handling and affordability. However, few or no long-term prospective clinical studies have been published to substantiate the claims that these materials' efficacy and biocompatibility are indeed comparable to MTA [42]. With many studies ongoing, the future looks hopeful for finding suitable substitutes for MTA.

A recent systematic review reports that Biodentine had significantly lower clinical and radiographic failure rates than formocresol (FC) at 12 months [10]. Several other systematic reviews report that MTA pulpotomy was superior to FC and FS, and all three treatments may be superior to CH pulpotomy [8, 9, 19]. Compared with FC, MTA reduced both clinical and radiological failures, with a statistically significant difference at 24 months for radiological failure. Compared to FS, MTA reduced radiographic failures at 24 months. Compared with CH, MTA reduced both clinical and radiological failures, with a statistically significant difference for clinical failure at 24 months [19]. This systematic review reported a 24 month success rates of 94% for MTA and 90% for Biodentine [19], while other systematic reviews have reported similar results at 24 months [8] and 18 months [46], concluding that this small difference has no clinical significance, as both materials have similar efficacy, and can be used safely according to the clinical situation and dentist's preference.

13.2 MTA/Biodentine Pulpotomy Procedure and Practical Considerations

With the use of local anesthesia, rubber dam and following complete caries removal, amputation of the coronal pulp, and attaining hemostasis, the pulp stumps are covered with MTA-like material prepared according to the manufacturer's instructions. The material is introduced carefully into the prepared cavity, avoiding trapped air bubbles and condensed using a wet sterile cotton pellet to ensure good adaptation to the cavity walls and margins in a layer of approximately 2 mm. After condensation, the MTA-like material can be covered with a less expensive alternative considering compatibility with the final restoration planned for that tooth, as illustrated in the following figures.

13.2.1 Pulpotomy of Single Tooth with MTA-Like Material

Figures 13.2, 13.3, 13.4, 13.5, 13.6, 13.7 and 13.8 illustrate the clinical procedure for a pulpotomy on a single tooth with a pre-mixed calcium silicate cement.

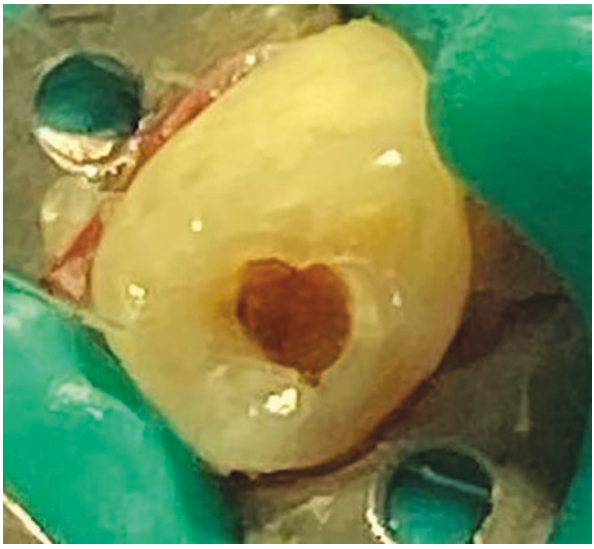

Fig. 13.2 Primary molar with deep caries and suspected caries exposure. Local anesthesia is applied and the tooth is isolated with a rubber dam

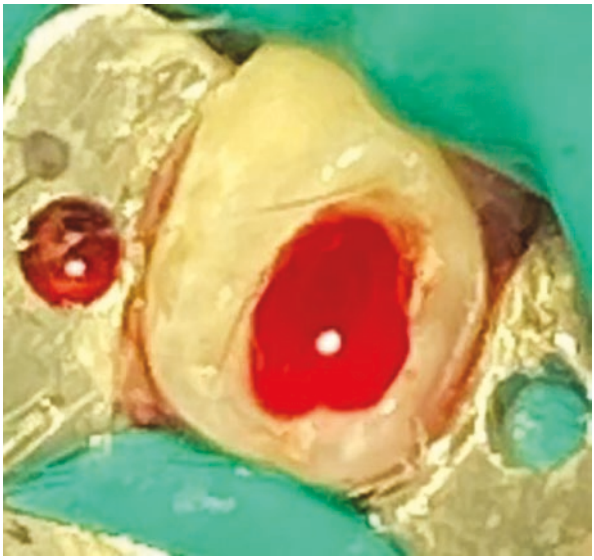

Fig. 13.3 After complete caries removal, pulp is exposed, roof of the pulp chamber is removed, and pulp tissue is completely removed

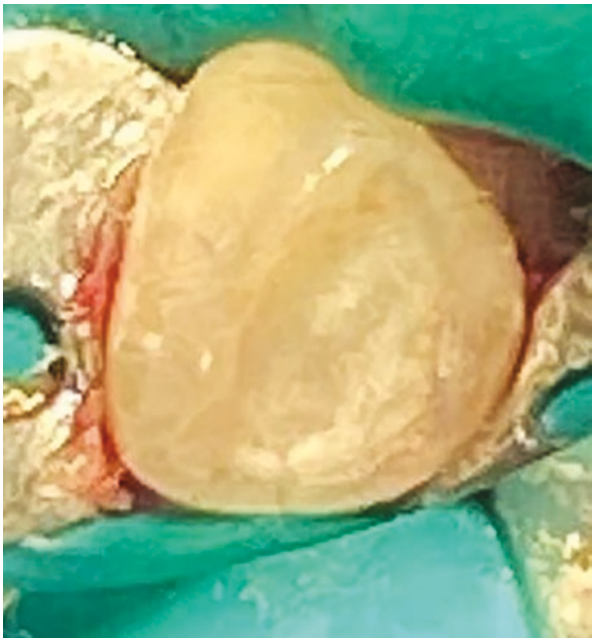

Fig. 13.4 Hemostasis is achieved using a cotton pellet (dry or moist with saline or water)

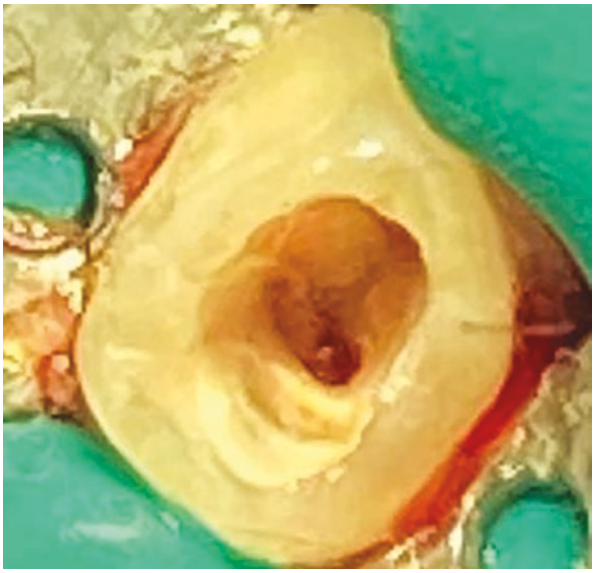

Fig. 13.5 Visible pulp canals after achieving hemostasis

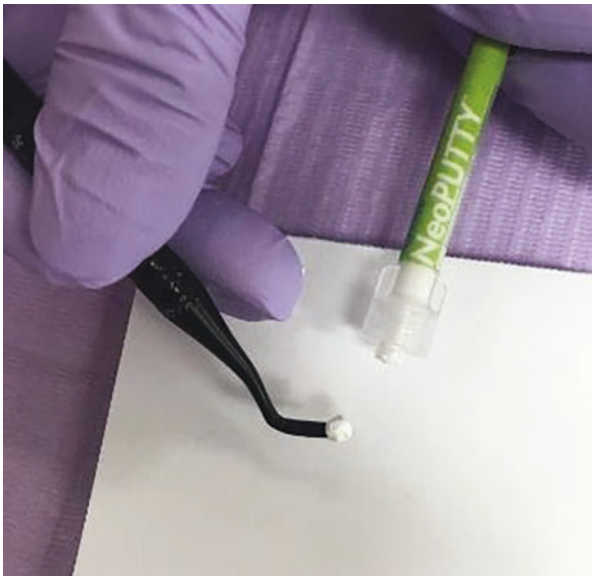

Fig. 13.6 Mix or prepare MTA-like material as per manufacturer's instructions. Illustrated is a pre-mixed, no-waste brand

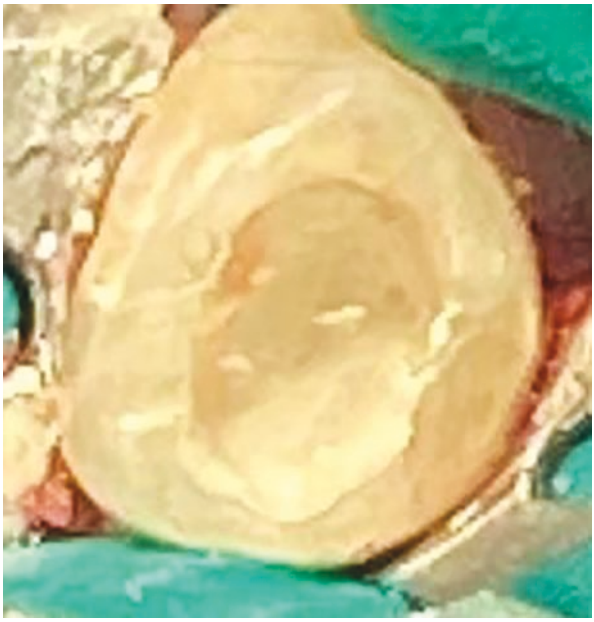

Fig. 13.7 MTA-like material is placed and condensed with a sterile wet cotton pellet, avoiding bubbles, ensuring complete coverage of the pulp canals and adaptation to the cavity walls in a 2 mm layer

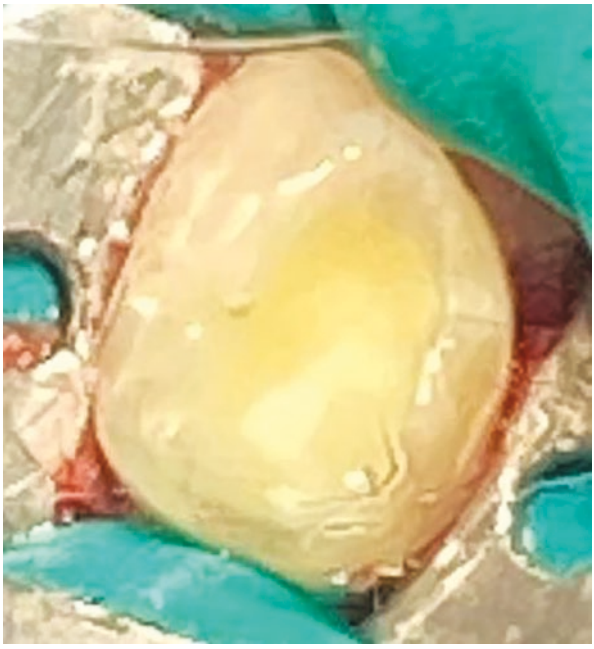

Fig. 13.8 MTA-like 2 mm layer is then covered with glass ionomer cement, or ZOE, ensuring compatibility of the material with the final restoration

13.2.2 Pulpotomy of Multiple Teeth with Biodentine

Figures 13.9, 13.10, 13.11, 13.12, 13.13, 13.14, 13.15 and 13.16 illustrate the clinical procedure for pulpotomies on multiple teeth with a pre-mixed calcium silicate cement (Biodentine).

The methods used for caries removal (bur or chemical), form of coronal pulp removal (bur or curette), hemostasis (dry or moist cotton pellet), and irrigation (water or saline) have not been found to have a significant impact on the success of the pulpotomy [19], so clinicians are encouraged to use their preferred techniques.

ZOE has traditionally been the material of choice for pulp chamber filling after pulpotomy is performed with materials including formocresol, ferric sulfate, or sodium hypochlorite. MTA and other similar materials create an excellent seal, but their high cost may limit the amount used at each procedure, so ZOE, reinforced ZOE, glass ionomers, or RMGIs can also be used to seal the rest of the pulp chamber without compromising treatment outcomes [19], as discussed in detail in Chap. 15.

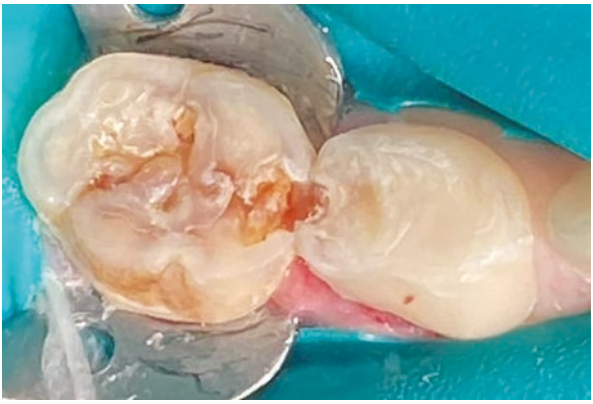

Fig. 13.9 Molars with deep caries in proximity to the pulp suspected of carious exposure, after local anesthetic and rubber dam isolation

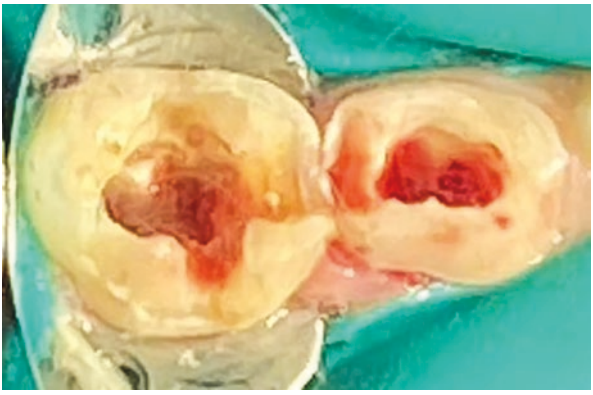

Fig. 13.10 Caries is removed completely and roof of the chamber is removed, as well as all pulp tissue in the chamber, exposing orifices of pulp canals

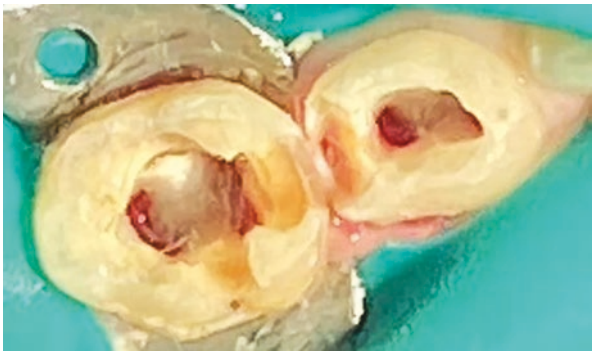

Fig. 13.11 Orifices for the pulp canals are visible after achieving hemostasis with cotton pellet

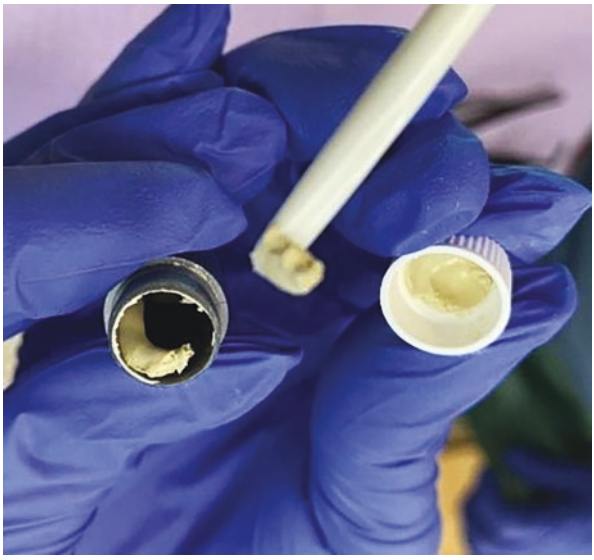

Fig. 13.12 Biodentine is mixed according to manufacturer's instructions

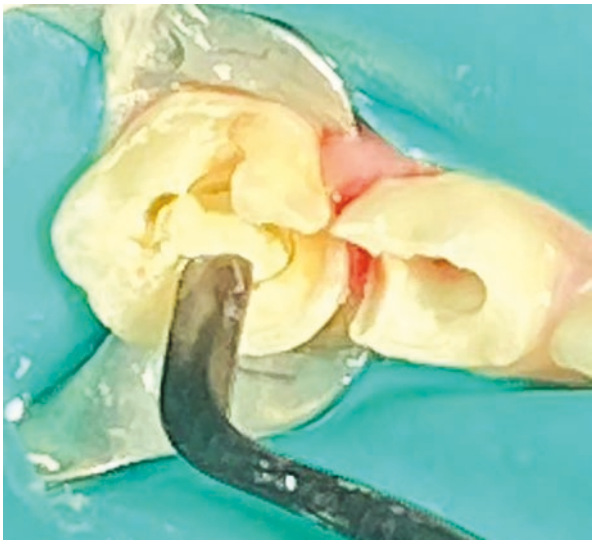

Fig. 13.13 Biodentine is placed in the pulp chamber

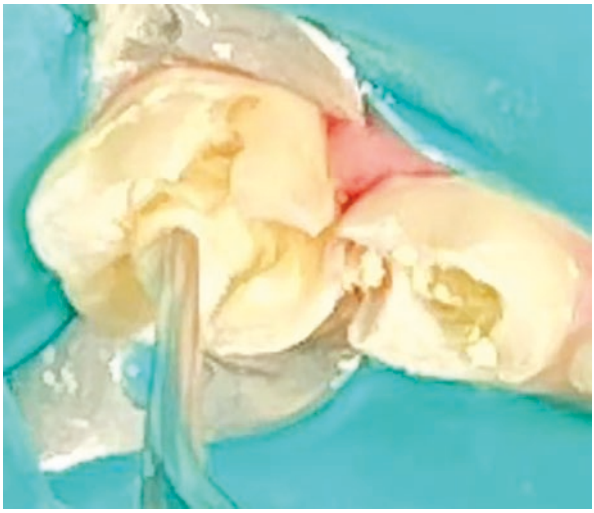

Fig. 13.14 Material is condensed with a sterile wet cotton pellet, avoiding bubbles, ensuring complete coverage of the pulp canals and adaptation to the cavity walls

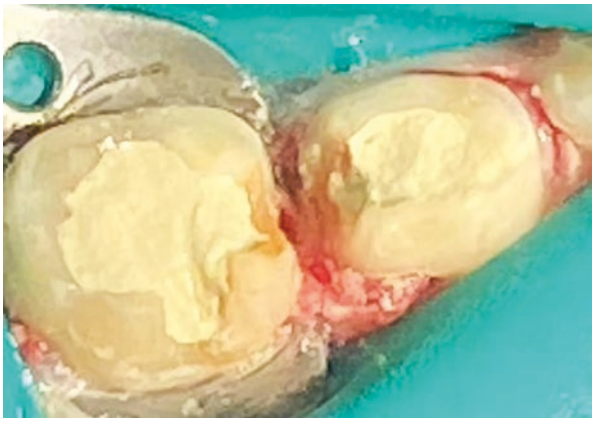

Fig. 13.15 Material in one capsule is enough to completely fill the whole pulp chamber of several teeth

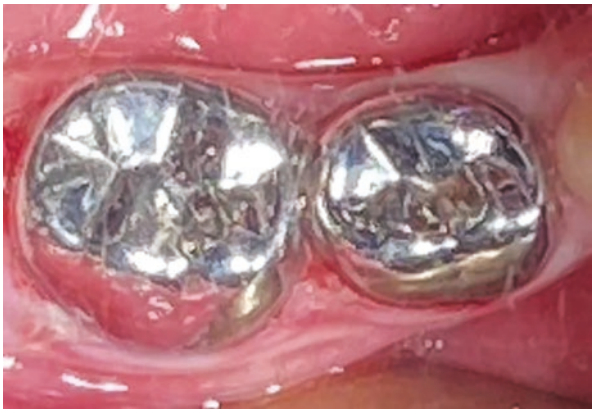

Fig. 13.16 Final restoration is placed, preferably on the same visit. Full preformed crowns are the preferred restoration on multi-surface lesions to ensure adequate seal

The high cost of the original MTA had traditionally been cited as the biggest barrier for its widespread use. As an example of this, one cost-effectiveness study in the UK cited it to be GBP 60 (approx. US $80) per pulpotomy at the time of the study 2006–2012 [53]. But new MTA-like materials that are more affordable may change the stage. A recent in vitro study [54] estimated the price of a treatment/dose of alternative MTA materials, when used in 2 mm layers over the pulp stumps. They report that the cost/dose of Biodentine is approx. $14.49, compared to $4.68 for NuSmile NeoMTA, $4.68 for New MTA Plus, $5.71 for MTA Angelus, and $13.75 for MTA-Flow. Their study cites the cost of gray ProRoot MTA is $26.51 and white ProRoot MTA is $31.25 (with prices calculated from companies' websites in 2017). They also calculate the cost of the material used for pulp chamber filling, and when combined, they report that NeoMTA-type cements and IRM powder-liquid base were the most affordable combination, being 3.5 less costly than using a bioceramic material followed by RMGI when used for a single pulpotomy. When multiple pulpotomies are done on the same visit (as may be the case with sedation or general anesthesia cases), the cost of Biodentine is lower, as one capsule can be used for multiple teeth filling the whole pulp chamber. Although only one of the factors to consider when planning for a pulpotomy, these price comparisons together with availability of the products are all important for the clinician to consider when choosing a material for pulpotomies in different settings. (See Chap. 11.)

13.2.3 Is There a New Gold Standard?

An umbrella review of systematic reviews reported that the highest quality of evidence for pulpotomy medicaments supports the effective application of MTA and formocresol [8]. The American Academy of Pediatric Dentistry (AAPD) guideline published in 2017 only recommended MTA and formocresol as medicaments of choice for primary teeth expected to be retained for 24 months or more, and they recommended against the use of calcium hydroxide. Other treatments, such as ferric sulfate, lasers, sodium hypochlorite, and tricalcium silicate, received only conditional recommendations [55]. A 2018 Cochrane review [9] concludes that MTA may be the most efficacious medicament to heal the root pulp after pulpotomy of a deciduous tooth and recommended more research to confirm an acceptable second choice, to overcome the toxicity concerns of formocresol.

As more recent randomized controlled trials including new materials are published, our knowledge may advance. A recent 2022 systematic review [19] performed a network meta-analysis to determine the rankings of the four top medicaments for pulpotomy success. Their results are that MTA was best, followed by Biodentine second, third was formocresol, and lowest was ferric sulfate. MTA was not significantly different from Biodentine but was significantly better than formocresol and ferric sulfate [19].

So which medicament should a clinician choose for pulpotomies? It seems from the latest research that MTA, Biodentine, and similar biocompatible materials offer the best efficacy at longer periods of observation and therefore, should be the

obvious choice. Although formocresol was the gold standard for decades, and its clinical efficacy had made it acceptable for a long time, toxicity concerns limit its use in many settings and many dental schools in the US and Europe no longer list it as the main agent taught and used for pulpotomy [56, 57], which will certainly have an impact on its future utilization. But long-term efficacy may not be the only factor a clinician is looking for when deciding on a pulpotomy medicament. The age of the patient and time of expected tooth survival may also come into play, together with affordability and availability of materials when deciding which material to use. It is up to the clinician to weigh in all factors including their own preferences and experience, to determine which choices are best for the specific situation, and to then explain to the parents the available options to obtain informed consent.

It is also important for the clinician to consider that the cost-effectiveness of the materials per tooth treated with pulpotomy may not be a determinant factor for cost savings in their overall practice. Studies have shown that the use of selective caries removal and indirect pulp therapy have significantly reduced the number of pulpotomy procedures without an increase in the number of abscessed teeth or extractions as a result [58]. With less pulpotomies performed, the cost of the material used could be slightly increased to a choice that can offer better success rates, without compromising cost-effectiveness.

13.3 Partial Pulpotomy for Primary Teeth

Partial pulpotomy is a procedure where only 1–2 mm of pulp tissue adjacent to the pulp exposure site are removed and the medicament is placed on presumably healthy tissue [59].

Partial pulpotomy for primary teeth has been a procedure described in numerous case reports, usually after trauma on anterior teeth, with varied success rates depending on the material used. One clinical study compared calcium hydroxide for partial pulpotomy for carious exposures on primary molars to formocresol pulpotomies and reported results of 74% success rates, similar to formocresol pulpotomy over 36 months [60]. Another randomized controlled trial that reports this technique for caries exposure on primary molars comparing MTA partial pulpotomy to formocresol pulpotomy reported overall success rates of 82% for MTA partial pulpotomy and 95% for formocresol pulpotomy over 24 months [61]. With the limited number of studies and the availability of better techniques and materials for pulpotomy with higher success rates over time, there is not enough evidence to recommend partial pulpotomies on primary teeth.

13.4 Treatment Planning for a Pulpotomy

Throughout the book, we have emphasized that diagnosis is crucial for the success of pulp therapy, and this is most important when planning for a pulpotomy. History of spontaneous pain, sensitivity to percussion, mobility of the tooth, presence of

sinus tract, or radiographic evidence of pathosis indicate that the inflammatory process has progressed beyond the confines of the involved tooth into adjacent tissues in which case, the likelihood for a successful pulpotomy is poor.

An umbrella review that included 9 systematic reviews published between 2014 and 2020 including 96 studies on different pulp treatments reported that at 24 months, indirect pulp capping had the highest success rate (94%), followed by direct pulp capping (88.8%), with different medicaments not significantly affecting the outcome. Pulpotomy showed the lowest success rate when all materials were evaluated together (82.6%) [8]. However, a more recent systematic review [19] that included new RCTs using bioactive calcium silicate cements and using only high-quality evidence found that IPT had 97% and 96% success at 24 and greater than 36 months, compared to pulpotomy, which showed 95% and 94% success at 24 and greater than 36 months. This slight difference was not found to have clinical significance, therefore recommending that both, IPT or pulpotomy using bioactive calcium silicate cements, are likely to have similar high success rates.

This new evidence is still consistent with the direction of this book, where we stress a conservative and biological approach to pulp therapy due to its consistent long-term results, but when considering the option of a pulpotomy, choose bioactive materials that are more likely to improve success over time.

It is evident that the indications for indirect pulp therapy are very similar to those for a pulpotomy: a vital primary tooth with deep caries and without signs of symptoms of irreversible pulpitis or necrotic pulp. If the indications are similar between both options, and it is recommended that a conservative approach should be taken, the clinician should first opt to choose indirect pulp treatment using selective caries removal to avoid pulp exposure whenever possible. So, when should a pulpotomy be chosen as the best treatment for a tooth, when establishing a comprehensive treatment plan?

Accurate pulp diagnosis is crucial for the success of vital pulp therapy. In young children, it is especially difficult to obtain an accurate diagnosis of vitality on a tooth with very deep caries, as pulp testing including cold and electric tests have shown to be reliable only in children older than 7 years [62], and history of pain may not give contributory information. Sometimes reference to pain may come from food impaction and not exclusively from pulpal origin. Clinical signs and symptoms (absence of pain to percussion and palpation) and radiographic evidence of healthy root, periodontal tissues, and periradicular bone aid ruling out pulp necrosis. But when the pulpal diagnosis is uncertain, that is, if radiographic decay shows the possibility of the decay process involving directly the pulp chamber in absence of a diagnosis of irreversible pulpitis or pulp necrosis, treatment planning a pulpotomy procedure may be a good option to verify the vitality of the pulp. This is especially the case if the child's cooperation requires advanced forms of behavior management like sedation or general anesthesia, since the option of retreating from a failed indirect pulp therapy would be complicated by the behavior challenge. Once caries removal has been completed with the result of a carious pulp exposure and the pulp chamber has been accessed, the clinician can evaluate the bleeding during pulp tissue removal and subsequent hemostasis to use as additional information to assess if

the radicular pulp may already be affected to confirm if pulpotomy is the best option, or if pulpectomy should be the treatment of choice.

In addition to an accurate diagnosis of pulpal status and the biological effect and success of the pulpotomy agent, obtaining a complete seal of the vital pulp from the oral environment is the third crucial element for the success of a pulpotomy. Therefore, the isolation used, the material used over the pulpotomy, the restoration type, and the experience of the clinician are factors that matter. The use of rubber dam isolation is considered the standard of care. Either a ZOE material, GI cement, or RMGI can be used over the pulpotomy agent providing adequate seal. Preformed metal crowns (PMCs or SSCs) seem to be the best option after pulpotomy, especially in multi-surface lesions. All these factors should be considered in light of the child's expected cooperation for treatment when planning for a pulpotomy. Ideally the final restoration should be completed on the same visit, however leaving the chamber sealed with ZOE, GIC, RMGI, or Biodentine as temporary fillings and completing the final restoration at a second visit do not seem to affect the success of the pulp therapy [19].

13.5 Conclusions

Our better understanding of the healing capacity of pulp tissue has changed the way we approach pulp therapy allowing us to use more conservative methods. When it comes to pulpotomy, the advent of new biocompatible and more affordable materials has improved our expectations of pulpotomy treatment allowing us to move forward after a century of compromising with materials with notable disadvantages. Bioactive calcium silicate materials (like MTA and Biodentine) have proven to have superior results over all other pulpotomy materials, and clinicians are encouraged to use them as the preferred medication for pulpotomies whenever possible.

Still, diagnosis, case selection, and proper management are key to the success of pulpotomy treatment. Future high-quality research based on uniform standards may present us with the evidence required to arrive at stronger recommendations and guidelines for pulpotomy treatment in the coming years.

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Non-Vital Pulp Therapies in Primary Teeth

14

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Contents

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14.1 Morphological Considerations

A major challenge for the clinician performing root canal treatment in primary teeth is the teeth's morphology. The primary dentition root and canal morphology includes a large range of anatomical alterations and is unpredictable [1, 2]. A new coding system for classifying the roots, canals, and developmental anomalies has been introduced recently [3]. This classification provides detailed information on tooth description, numbers of roots, and root canal configuration in addition to accessory canals and tooth anomalies [3].

Root canal configurations change dynamically with increasing age as the deposition of dentine and physiologic root resorption alter the morphology of the root apex, leading to difficulty in working length determination. Accessory canals are common in the primary dentition, especially in the furcation area [4–8]. Treatment of accessory canals in a clinical setting is advisable only when the primary tooth is not about to exfoliate or if there are no signs of extensive root resorption.

14.2 Primary Tooth Root Canal Physiology

Incisors and canines are usually single rooted with a single root canal [8] but accessory roots and root canals in primary anterior teeth have been documented [3]. Primary maxillary central and lateral incisors normally have a single conical or triangular-shaped root and a large single canal while primary maxillary canines normally have a single, triangular-shaped root and a large single canal. Primary mandibular canines typically have a single, conical root that tapers toward the lingual and a large single canal [8]. Primary anterior teeth after pulpectomies had a higher survival rate than primary molars [9].

Primary maxillary molars (Fig. 14.1) may have two to four roots, with the three-rooted variant being the most frequent. Fusion of the distobuccal (DB) root with the palatal root is also common as a double-rooted variant [8]. The prevalence of a second mesiobuccal (MB) root canal can be as high as 95% [10]. The palatal root is the longest and is curved, followed by the MB root. The DB root is the shortest and smallest in diameter of the three roots [8]. The maxillary primary first (Fig. 14.1) and second (Fig. 14.2) molars have three divergent and separated roots [1]. Maxillary first molars have three canals, and second molars have either three (70.9%) or four canals (29.1%).

The primary maxillary second molar (Fig. 14.2) normally has three roots that are widely separated. The palatal root is the longest followed by the MB root. The DB root is the shortest and roundest of the three roots. Each root usually contains a single canal system [8]. In maxillary molars, the double root variant with fusion between both the distobuccal and palatal roots is the predominant type, in the first molar it ranges from 60 to 77%, and in the second molar it is 22.5% [11]. In the mesiobuccal roots of the maxillary molars, a double canal system was observed [12].

While primary second molars, both in the maxilla and in the mandible, are more accessible than first molars, all of them are negotiable [13].

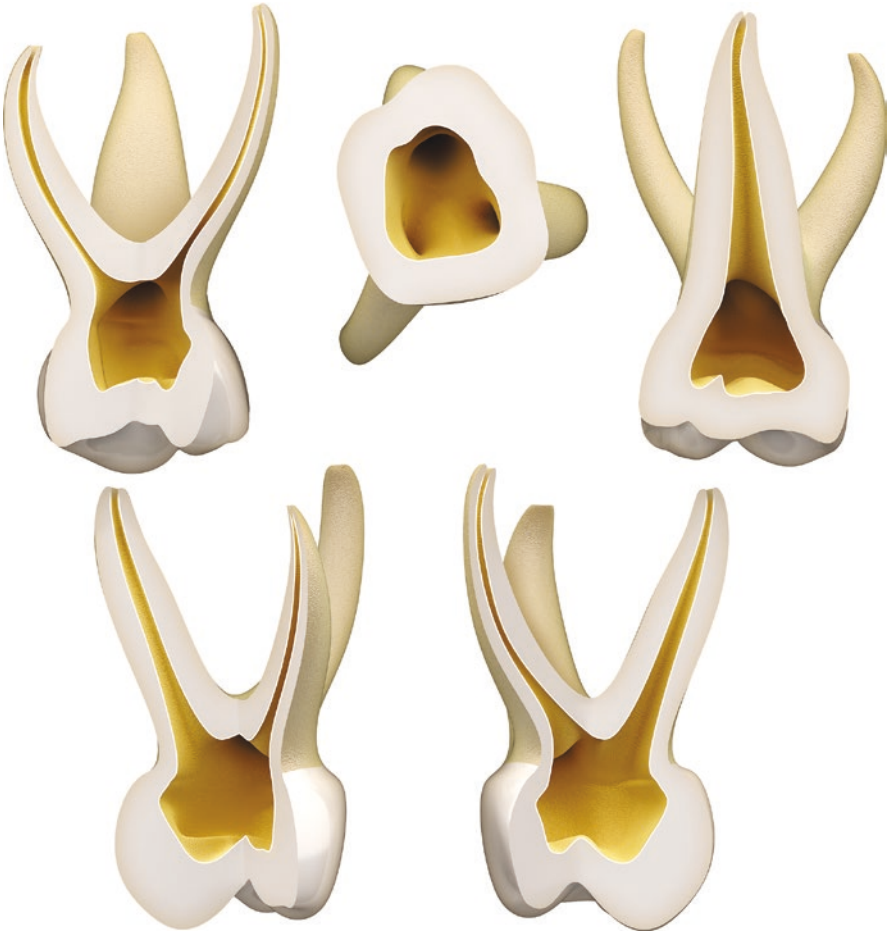

Fig. 14.1 Maxillary first primary molar, internal morphology (upper row, buccal occlusal and palatal view; lower row, mesial and distal views)

Primary mandibular molars (Figs. 14.3 and 14.4) can have one to four roots; the double-rooted variant is the most common [8, 12, 14]. Two canals in the mesial root and one canal in the distal root comprise the most observed anatomical configuration [14]. Internal and external morphology of the primary mandibular first molar (Fig. 14.3) closely resembles that of the primary mandibular second molar (Fig. 14.4) [1]. Mandibular primary first molars have either three canals (79.2%) or four canals (20.8%), and all second molars have four canals [13]. A double canal system was observed in the mesial roots of the mandibular molars [12].

It is important to note that documented root canal morphology varies with the diagnostic aid used (e.g., Cone beam CT) and in different ethnic populations [11].

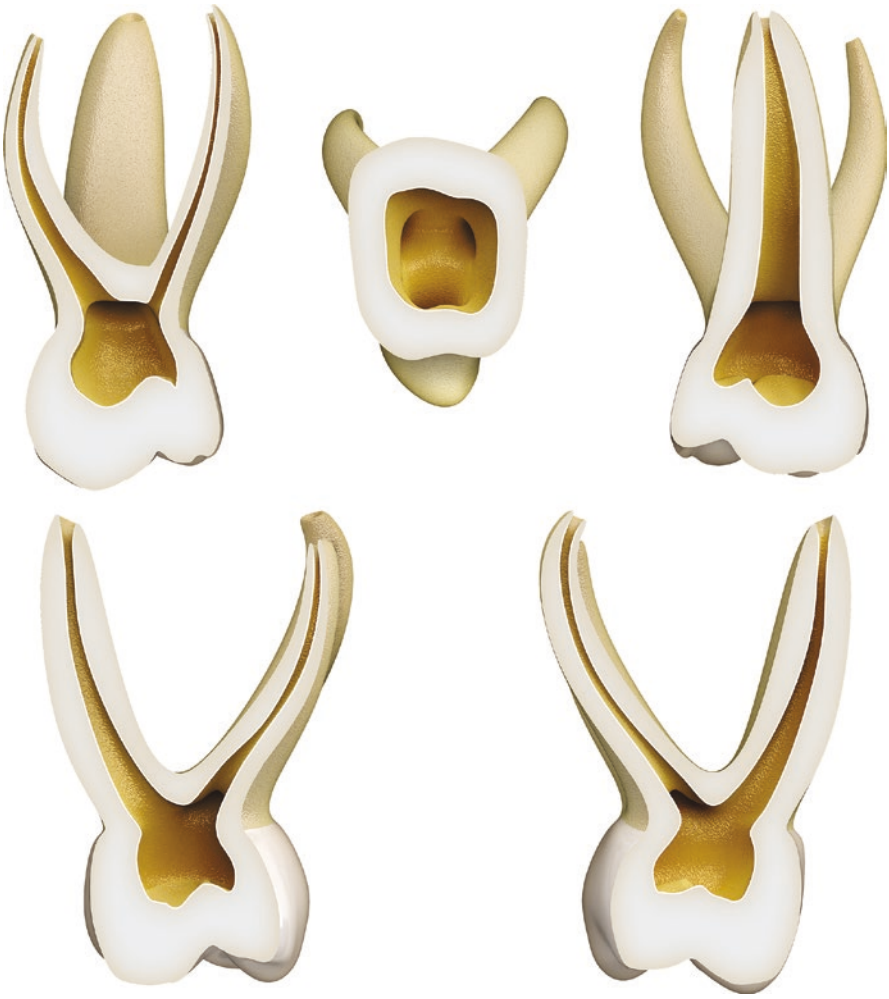

Fig. 14.2 Maxillary second primary molar, internal morphology (upper row, buccal occlusal and palatal view; lower row, mesial and distal views)

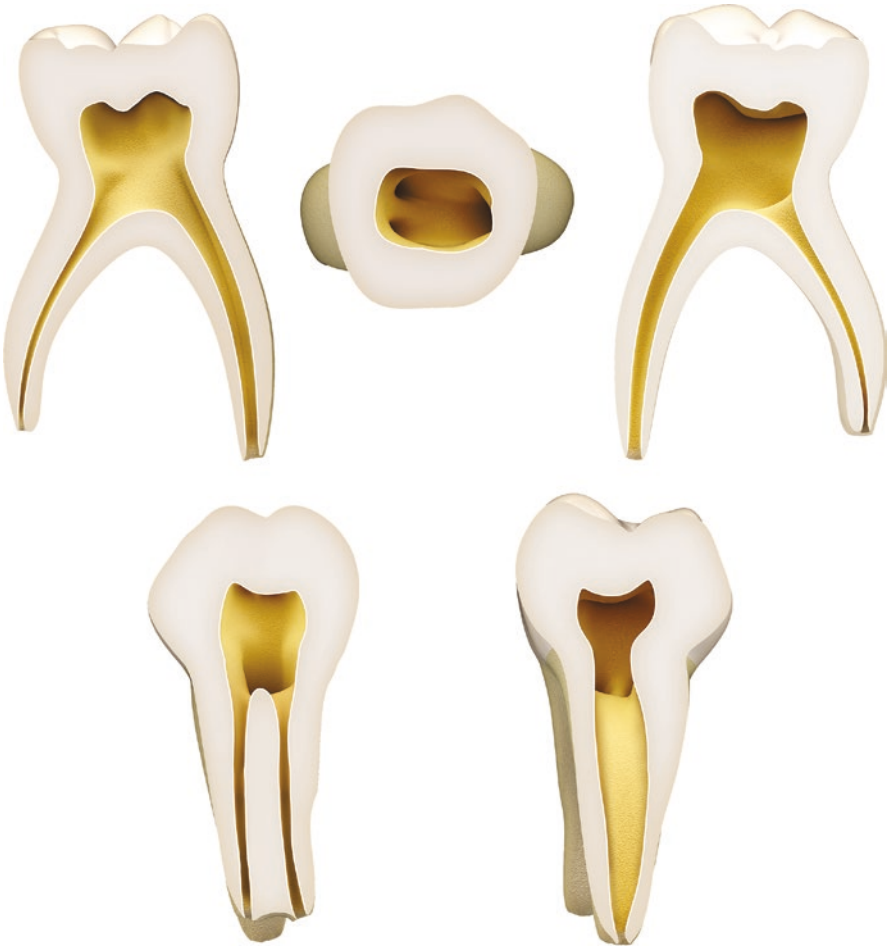

Fig. 14.3 Mandibular first primary molar, internal morphology (upper row, buccal occlusal and palatal views; lower row, mesial and distal views)

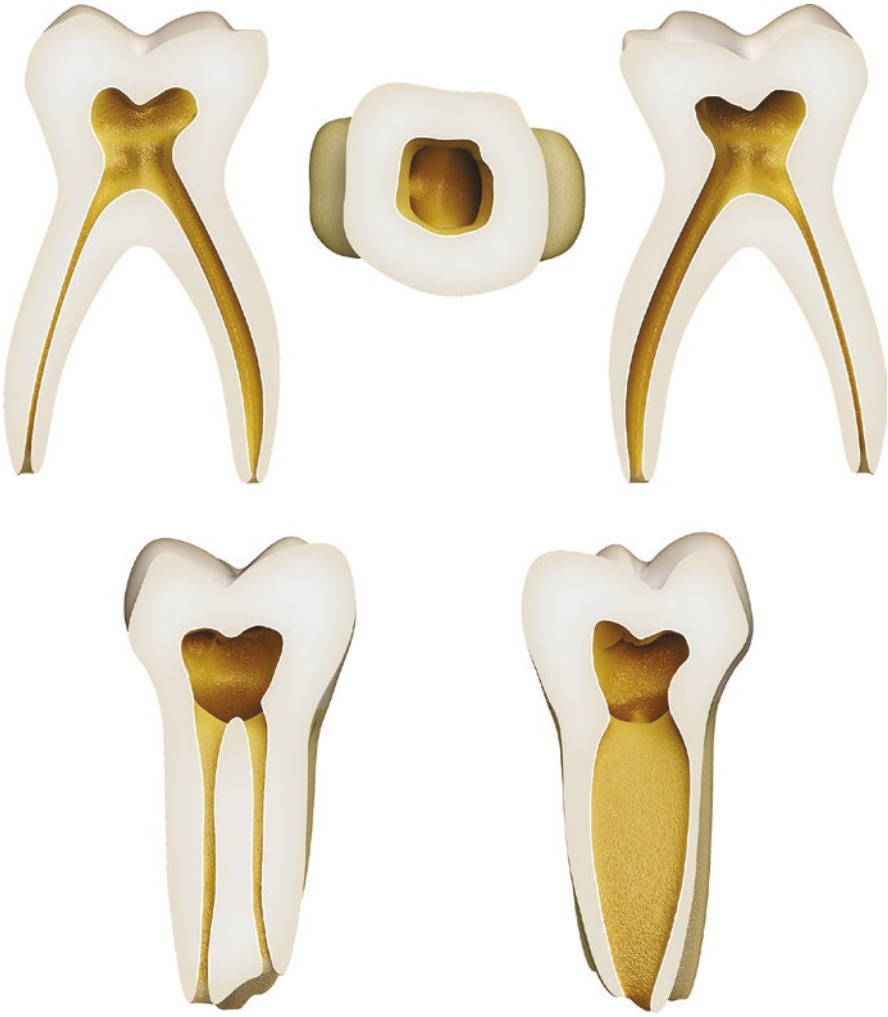

Fig. 14.4 Mandibular second primary molar, internal morphology (upper row, buccal occlusal and palatal views; lower row, mesial and distal views)

14.3 Primary Tooth Root Canal Anomalies

Unusual and complicated morphology of the primary tooth root canals make cleaning and shaping them difficult and reduce the success of root canal therapy for primary teeth [15]. The physiologic procedures of root resorption, which starts soon after the complete formation of the root, and the continuous formation of secondary dentine, modify the root canal system over time. The resorptive process along the root surface is uneven and is subject to continuous morphological changes [16].

Nearly 83% of extracted primary molars had at least one accessory canal in the furcation area (chamber/furcation canals) [3]. Mesial and distal roots of primary second mandibular molars have lateral canals [17]. Only a small number of those canals are patent, and the majority usually terminate within the root dentine.

Another anatomic root variation in molars is the presence of extra roots. Primary mandibular first molars usually have one mesial and one distal root, but rarely an additional third root (supernumerary root) is seen. When it is located distolingually to the main distal root, it is called "radix entomolaris (RE)" [18, 19], and when it is placed mesiobuccally to the mesial root, it is called "radix paramolaris (RP)" [20]. Anatomic variations such as taurodontism [21], root fusion, dens invaginatus [22], enamel pearls [23], and C-shaped canals have been seen in mandibular molars.

14.4 Pulpal and Periapical Diagnostics

Pulp condition should be evaluated based on the clinical signs and symptoms the patient presents with, and on oral and radiographic examination, as explained below and in Chap. 9. Pre-and post treatment radiographic control is crucial [24].

14.5 Indications for Pulpectomy

A pulpectomy is indicated in primary teeth with irreversible pulpitis or necrosis. Clinically, a tooth in which the pulp chamber has been opened (for pulpotomy) and the radicular pulp exhibits clinical signs of irreversible pulpitis or pulp necrosis (e.g., suppuration, purulence) will require a pulpectomy. Radiographic examination of the roots should exhibit minimal or no resorption. When there is no root resorption present, pulpectomy is recommended over lesion sterilization tissue repair (LSTR) [25, 26]. Pulpectomy is a viable long-term treatment for non-vital teeth without root resorption compared to those with root resorption. Therefore, pulpectomy should be considered for non-vital primary teeth without preoperative root resorption [26].

Diagnosis of irreversible pulpitis cannot be based solely on pulp tissue bleeding that cannot be controlled within 5 min [27] and needs to be based on at least one of the signs or symptoms that indicate irreversible pulpitis or pulp necrosis in primary teeth: unprovoked toothache, sinus tract or other soft tissue pathology, gingival swelling not associated with periodontal disease, abnormal tooth mobility, radiographic furcation or periapical radiolucency, or external or internal root resorption [27, 28].

Pathological changes in alveolar bone because of pulpal inflammation typically are located in the furcation region of the primary molars as opposed to the periradicular region in the permanent molars [8].

14.6 Contraindications for Pulpectomy

In non-vital primary teeth, the clinician should choose extraction over non-vital pulp therapy for teeth deemed non-restorable that have an inadequate crown or extensive root structure resorption.

Unrestorable teeth are characterized by at least one of the following: high mobility of the tooth (mobility grade III), inadequate bone support, obliteration of the root canal, a pathological lesion extending to the successor's tooth germ, evidence of extensive internal/external pathological root resorption, or less than two-thirds of the root intact [24]. Pulpectomy is a viable long-term treatment for non-vital primary teeth without root resorption but is less successful for those with root resorption.

14.7 Pulpectomy Procedures

Clinicians may choose either a single-visit or two-visit pulpectomy based on clinical expertise and individual circumstances [26, 29]. We describe here a single-visit procedure [30].

14.7.1 Access and Debridement

Under local anesthesia and rubber dam isolation, caries is removed, and the pulp chamber is accessed. The use of a rubber dam for non-vital procedures is accepted as the standard of care as it is important to maintain isolation from saliva, blood, and other contaminants [29]. Figure 14.5 demonstrates mandibular first and second

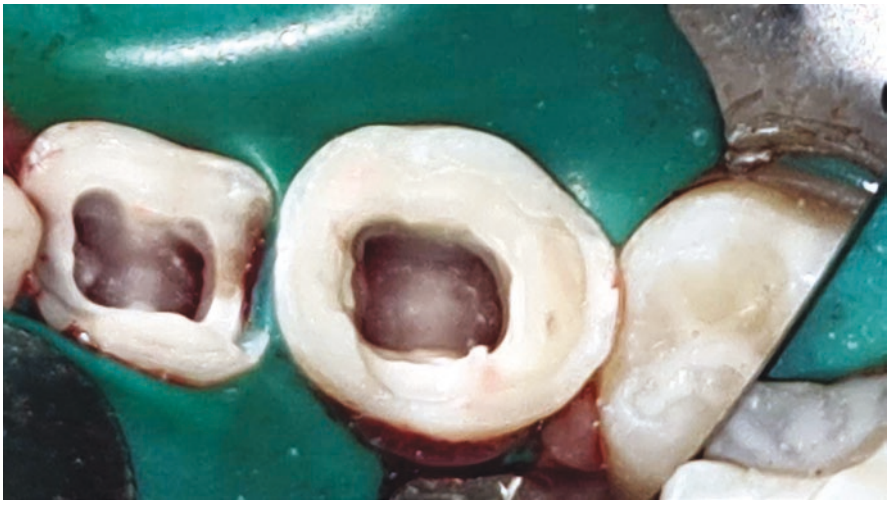

Fig. 14.5 Mandibular first and second primary molars opened for pulpectomy, showing the orifices of the canals

primary molars opened for pulpectomy, showing the orifices of the canals. The most common cause of inaccessibility of primary teeth to pulpectomy is unsuitable entrance cavity. It is followed by tortuous canals and orifice calcification. Maxillary first molar (Fig. 14.1) is the most frequently reported as inaccessible. The least frequently reported is the mandibular second molar (Fig. 14.4). The distobuccal canal of the maxillary first molar and the mesiolingual canal of the mandibular first molar are the most frequently inaccessible canals [15].

After the pulp, inflamed or necrotic, is removed, access preparation is refined to make sure that entrance to all the canals is possible and clearly visible. When each canal orifice has been located, a properly sized barbed broach used to extirpate the pulp tissue is selected. The broach is used gently to remove as much organic material as possible from each canal. Endodontic files are selected and adjusted to stop 1–2 mm short of the radiographic apex, with the preliminary working length estimated according to the preoperative radiograph [31] and/or to the apex locator [14]. Clinicians may choose any of the methods (tactile, radiographs, apex locators) based on their clinical expertise and individual circumstances [26]. The instruments should be slightly bent to adjust to the curvature of the canals, thus preventing perforations on the outer and inner portions of the root [32]. It is important to keep in mind that primary molar roots are usually curved to allow for the development of the succedaneous tooth. During instrumentation, these curves increase the chance of perforation of the apical portion of the root or the coronal one-third of the canal into the furcation [32].

14.7.1.1 Instrumentation Technique

The main goal of canal instrumentation is the removal of organic debris [33]. Mechanical clearing of remnants from the canal is performed with a series of 21 mm long K-type endodontic files (Unitek Corp., Monrovia, CA) up to file No. 30 or 35. It is imperative to avoid access shaping of the canal that might lead to perforation in the furcation or the lateral walls.

Some dentists prefer to use nickel titanium files placed in a special rotary handpiece for root canal debridement. This facilitates root canal instrumentation, especially in canals that are difficult to negotiate with hand instruments. Cautious manipulation is important, however, to prevent breaking the file or over-instrumenting the canal and apical tissues. Rotary instrumentation decreases instrumentation time [29, 34–36], extent of dentine removal [34], and postoperative pain (due to the lesser amount of periapically extruded debris which triggers inflammatory process) [36] and tends to result in more flush fills [29].

Several comparisons of instrumentation techniques showed that manual instrumentation with K files resulted in significantly more dentine removal when compared to rotary instrumentation [1, 34], but a recent, cone-beam computed tomography-based in vitro analysis of primary root canals found no significant differences between rotary and manual files. Yet, the researchers concluded that the rotary files showed better performance, as a significant difference was found at the middle level of the root and attributed this finding to the difference in the file design itself [37].

A meta-analysis on optimal or flush filling to the root's apex of primary tooth root canals in vivo showed no statistical difference but favored rotary files achieving more flush apical fills [29, 33]. Overall, the use of rotary instruments yielded 32% more flush fills than those using manual filing [29].

Intracanal separation (breakage) of nickel-titanium rotary instruments is still a major concern of endodontists, with a consequent possible reduction in the outcome rate [38].

In summary, the preparation of canals with rotary files can be an alternative to conventional files in primary teeth. Rotary instrumentation time was significantly shorter than manual by approximately 2 min, but the two instrumentation methods had comparable successes while the occurrence of flush fills favored rotary. Considering these findings and the additional resources/training for rotary over manual instrumentation, clinicians may choose either method of instrumentation [26].

Er,Cr:YSGG laser provided similar cleanliness as rotary instrumentation technique and was superior to manual instrumentation [39]. The laser technique required less time for completion of the cleaning and shaping procedures when compared with both rotary and hand instrumentation [39]. One should be cautious not to use laser technique when the patient is on inhalation sedation as it is prohibited by the manufacturer due to the risk of sparks from the laser machine in proximity to oxygen from the nitrous oxide.

14.7.2 Root Canals Irrigation

Regardless of the filing system used, non-instrumented areas still exist [35]; The complex internal anatomy of primary molars results in zones that are inaccessible to debridement, such as accessory canals, ramifications, and dentinal tubules [40]. While such zones are missed by instrumentation, irrigating solutions synergize mechanical debridement by dissolving tissue and disinfecting the root canal system and are crucial for lubrication and flushing away of necrotic and contaminated materials [41–44]. Clinically effective and biocompatible irrigants can significantly reduce (or even eradicate) the microorganisms and their by-products in the pulp canals [40, 44]. Currently, there is no agreement on the best intracanal irrigant solution for use against pulp pathogens involved in irreversibly inflamed/infected or non-vital primary teeth [40].

An ideal irrigant must have a broad antimicrobial spectrum and high efficacy against anaerobic and facultative microorganisms, be able to dissolve necrotic pulp-tissue remnants, inactivate endotoxins, either prevent the formation or dissolve the smear layer during instrumentation, and be non-toxic (to periodontal tissues), non-caustic, and non- allergenic [43, 44].

A major concern in root canal treatment of primary teeth is the proximity of the permanent tooth germs, which might be affected if the cleanser material is extruded beyond the physiologically resorbing apex [43]. An in vitro study showed that

irrigant was extruded apically in teeth with open apices by both syringe and endosonic methods. There was no significant extrusion of irrigant in teeth with closed apices [45].

Clinicians are especially cautioned in the use of sodium hypochlorite (NaOCl) for irrigation, as significant morbidity has been reported when this irrigant is extruded past the apices of primary teeth [46–48]. NaOCl is a weak alkaline/base that acts on the remains of pulpal tissue, food, and microorganisms, denaturing and dissolving them in water. It is best known for its strong and rapid antibacterial activity even at low concentrations. NaOCl at 0.5–1% is recommended for use in canal irrigation instead of the 5.25% solution [26, 43]. Er:YAG laser use with NaOCl decreased *E. faecalis* slightly more than NaOCL alone [49].

Other intracanal irrigants have been proposed for primary teeth, such as chlorhexidine gluconate, ethylenediaminetetraacetic acid (EDTA), and citric acid. Chelating agents can be used in conjunction with irrigants: EDTA is an agent used for the removal of the inorganic portion of the smear layer that has little if any antibacterial activity [50]. Citric acid 6% and EDTA can effectively remove the smear layer created during canal instrumentation [51, 52]. Pulpectomy outcome was improved by smear layer removal using 2.5% sodium hypochlorite (NaOCl) and 6% citric acid [51], but there is controversy whether removal of the smear layer improves pulpectomy results [51, 52]. BioPure MTAD Antibacterial Root Canal Cleanser (a mixture of tetracycline isomer, acid, and detergent, Biopure, Tulsa Dentsply, Tulsa OK, USA) is a final irrigant for smear layer removal recommended for use with patients over the age of 8 years. It has been proved to be effective in eliminating resistant microorganisms and providing sustained antimicrobial activity [53].

Hydrogen peroxide solution was used for many years as an endodontic irrigant. It is active against viruses, bacteria, yeasts, and even bacterial spores, but there is no evidence supporting its use as an endodontic irrigant [40, 43].

Chlorhexidine (CHX) gluconate has a wide antimicrobial spectrum and is effective against Gram-positive and Gram-negative bacteria and yeasts. It absorbs onto the cell wall of the microorganisms and causes leakage of the intracellular components. At high concentrations, chlorhexidine gluconate has a bactericidal effect due to the precipitation and/or coagulation of the cellular cytoplasm. When used in identical concentrations, NaOCl and CHX had a similar antibacterial effect in the root canal and infected dentine, but CHX lacks the tissue-dissolving ability [43].

In recent years, the risk of allergy to chlorhexidine is increasingly recognized [54], yet it has not been described in pulpectomy procedures.

Systematic reviews showed no impact of irrigants—sodium hypochlorite one to 5%, water/saline, or chlorhexidine—on pulpectomy success [25, 26]. Therefore, clinicians may choose any of these irrigation solutions based on their clinical expertise and individual circumstances [26].

It is recommended to irrigate with normal saline prior to drying the canals with appropriately sized sterile paper points.

14.7.3 Filling the Root Canal(s)

An ideal root canal filling material should resorb concurrently with the physiologic resorption of the roots and be nontoxic to the periapical tissues and the permanent tooth bud. It should resorb readily if forced beyond the apex and be antiseptic, easy to insert, non-shrinkable, and easily removed if necessary [55]. In addition, it should be easily placed, not set to a hard mass that could deflect an erupting permanent tooth [52], be radiopaque and not discolor the tooth, adhere to the walls, and not shrink [56].

Most root filling materials for primary teeth contain resorbable materials, such as calcium hydroxide (CH), non-reinforced zinc oxide eugenol (ZOE) [57, 58], and iodoform. We discuss here the main characteristics of several popular materials and focus on their mode of action and biocompatibility.

Except in anterior primary teeth, CH is always used in combination with another filling material, such as iodoform or ZOE [59–61]. Several root canal filling materials combine iodoform and calcium hydroxide [62]. Calcium hydroxide provides a high pH (>10) environment that, along with iodoform, creates an increased bacteriostatic effect [61]. Vitapex™(Neo Dental International Inc., Burnaby, British Columbia) and Metapex™(Meta Biomed LTD, South Korea) are both in a premixed syringe, contain mostly iodoform and CH (see Table 14.1 for details), and are radiopaque. Both are resorbable and hence preferable in primary teeth. When extruded into furcal or apical areas (Fig. 14.6 shows such extrusion in a mandibular left second primary molar with four canals), they can either diffuse or be quickly resorbed by macrophages and do not cause a foreign body reaction. Figure 14.7 shows pulpectomy using Metapex in the maxillary first left primary molar demonstrating three canals filled loosely with the material.

Table 14.1 A description of various root sealers for primary teeth

Root filling material	Calcium hydroxide with iodoform	Calcium hydroxide (for anterior primary teeth)	Zinc oxide-eugenol	Iodoform-based	Zinc oxide and iodoform
Materials	Vitapex™ (Neo Dental International Inc., Burnaby, British Columbia) Metapex™ (Meta Biomed LTD, South Korea)	Sealapex™ (Kerr, Brea, CA, USA) Calcicur™ (VOCO, Germany)	Pulpodent™ (VladMiVa, Bucaramanga, Colombia)	Metapex™ (Meta Biomed Co., Ltd. Cheongju City, Korea) Kri paste™ (Pharmachemie AG, Zurich, Switzerland)	Maisto paste™ (Inodon, Porto Alegre, Brazil) Endoflas™ (Sanlor FS, Columbia South America)

Table 14.1 (continued)

Root filling material	Calcium hydroxide with iodoform	Calcium hydroxide (for anterior primary teeth)	Zinc oxide-eugenol	Iodoform-based	Zinc oxide and iodoform
Introduction into the root canal	Disposable tips or spiral lentulo mounted on a slow speed handpiece	Spiral lentulo or auto mix syringes or application cannula	Without setting accelerators may be pushed into the root canals using a root canal plugger	Sterile syringe with disposable plastic needles	Spiral lentulo mounted on a slow speed handpiece
Problems	Aqueous vehicles cause depletion of paste from root canals before time of physiological tooth replacement [63]. Viscous vehicles promote lower solubility of the paste. Oily vehicles have lowest solubility and diffusion of calcium hydroxide pastes [64]		Tends to resorb at a slower rate than the roots of the deciduous teeth [65–67]	Minimal antibacterial activity against most pure cultures [68] Overfilling and voids [69]	
Anti-bacterial activity	No antibacterial activity against most pure cultures [70]		Strong antibacterial effectiveness [70, 71]	Kri paste showed stronger antibacterial effectiveness than ZOE [71]	

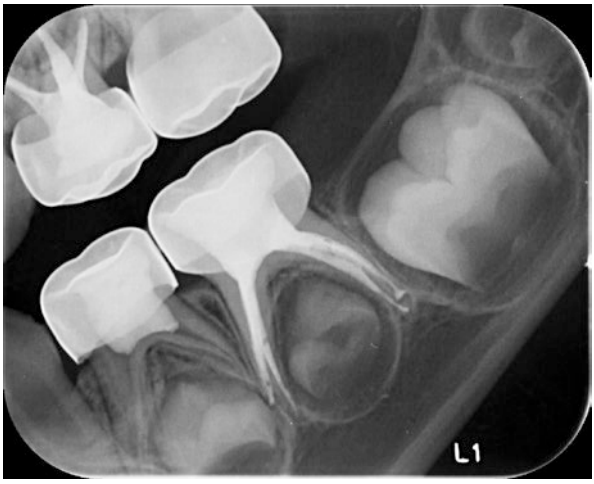

Fig. 14.6 Pulpectomy using Metapex in the mandibular second left primary molar demonstrating four canals filled loosely with the filing material extending slightly beyond the apex

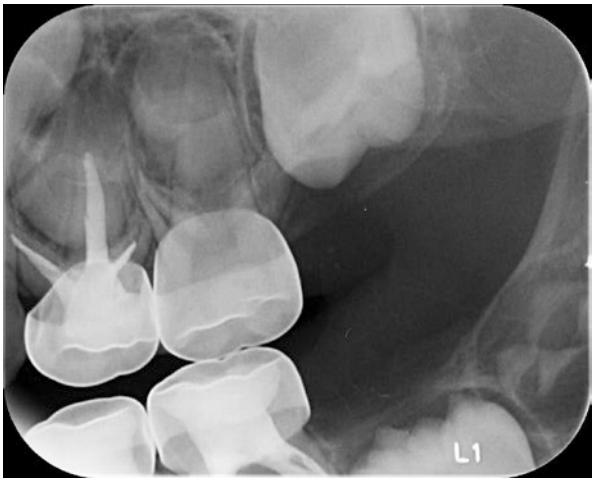

Fig. 14.7 Pulpectomy using Metapex in the maxillary first left primary molar demonstrating three canals filled loosely with the material

CH pastes (Calcicur™, by Voco America Inc., USA; Apexit Plus™by Ivoclar Vivadent AG, Schaan, Liechtenstein; and Sealapex™ by Kerr Corp., USA) for anterior teeth pulpectomies can be used either in premixed syringes or mixed as a powder and water. Contrary to CH that does not cause discoloration, iodoform-containing filling materials may cause discoloration in the coronal part of the teeth [72] especially when used in anterior primary teeth.

Non-reinforced zinc oxide-eugenol (ZOE) is another popular root canal filling material. For primary teeth pulpectomy, zinc oxide powder is mixed with eugenol to a creamy or thick consistency which is radiopaque. In teeth with irreversible pulpal changes pulpectomies with ZOE or Endoflas™(Endoflas™ contains ZO/iodoform/CH, i.e., ZOE plus iodoform plus calcium hydroxide) gave similar outcomes to Vitapex™ and Sealapex™, although there was no agreement with regard to filling materials' resorption [73]. Overfilling and voids were more commonly seen in teeth filled with Metapex™ [69]. There was no significant difference between Endoflas™, Metapex™, and ZOE in pulpectomy success rates. The decreased use of ZOE nowadays may reflect the concern that it is non-resorbable and may prevent timely root resorption of the exfoliating tooth. In addition, extruded ZOE might cause a foreign body reaction [61].

Iodoform-based paste, KRI paste™, demonstrated higher success rates (84%) than ZOE (65 %) [61, 74]. ZO/iodoform/CH or ZOE maintained an 18-month success rate approximating 90% over time while iodoform success decreased to 71% or lower over time [26, 29]. Using iodoform-based filling material for pulpectomy of primary teeth, like the one used in Brazil known as the Guedes-Pinto™ (GP) paste composed of iodoform, camphorated paramonochlorophenol (PMCC), and a dermatological ointment containing prednisolone acetate and rifamycin [75], is not well supported in the literature.

Based on these findings, $Ca(OH)_2$/iodoform is recommended for pulpectomy in primary teeth nearing exfoliation while ZOE-containing pastes should be utilized when exfoliation is not expected to occur soon [76].

The evidence suggests that ZO/iodoform/CH and ZOE may be a better choice for pulpectomy success compared to iodoform at 18 months. Meta-analysis after 18 months showed that ZO/iodoform/CH ranked first followed by ZOE and then iodoform [26].

Chairside mixed materials are more time-consuming and technique-sensitive than those that come in a syringe. Also, the material must be carried into the canal with a lentulo or rotary instrument that may break inside the root canal, especially in primary teeth with tortuous root canals. In case of a broken instrument in the canal, one should consider extracting the tooth or performing a close follow-up and extracting the tooth as soon as the tooth bud is approaching the edge of the lentulo revealed by the resorbing root.

The instruments that are used to fill the canals vary according to the type of filling material. Thick pastes such as ZOE are inserted and condensed with root canal pluggers, while diluted pastes like iodoform and calcium hydroxide-based materials are inserted with a spiral lentulo mounted on a slow speed engine. Other materials are inserted by plastic syringes and tips provided by the manufacturer. A final X-ray is necessary to evaluate the filling of the canals and ensure no overfilling that might damage the permanent tooth germ [24].

The quality of the root canal fill (flush fill—a canal filled to the apex) and pulpectomy success using lentulo spirals, hand pluggers, and syringes were not statistically different [29]. Two studies comparing different methods for filling the canals showed differing results. Using a spiral lentulo resulted in 63–91% flush fills versus 48–87% with a hand plugger and 62–87% with a syringe. In both studies, there was no significant difference ($P = 0.13$, $P = 0.66$) between the three methods of obturation in achieving pulpectomy flush fills [25, 29, 77].

Overfilling of the canals appears to be related to a lower success for pulpectomy [29]. Some techniques may cause more overfills (lentulo spiral) than others [25, 26, 77]. Metapex fillings showed more overfilling and voids than Endoflas and ZOE [24].

14.8 Supplementary Methods

Dental operating microscopes, electronic apex locators, rotary nickel-titanium files, and irrigation techniques are at the front of the endodontic armamentarium today [14, 31, 78].

The use of a dental operating microscope is not essential when treating primary teeth [14], as contrary to permanent teeth, preparation of root canals in primary teeth is based on chemical means rather than on mechanical debridement [31].

14.8.1 Electronic Apex Locators

Besides their essential role in preoperative evaluation, radiographs are the most prevalent method for measuring the working length in primary teeth [14]. Electronic apex locators can serve as an adjunct means to overcome the two-dimensional limitations of the radiographic image and reduce both radiation exposure and processing time, making the treatment more convenient to both the operator and the child. They can also help detect root perforations resulting from internal or external root resorption [14]. There is controversy if the use of apex locators is superior to the radiographic method [79–81], as no statistically significant differences were found between radiographic image and apex locator lengths [82].

While early research claimed that the physiological resorption in primary teeth compensates apex locators' performance [83], limiting them for use only as an addition to other diagnostic measures [63], more recent studies have shown that they can give accurate results in primary teeth [26, 84]. The presence of root resorption did not affect the accuracy of the measurement [85].

Specifically, Root ZX™ mini apex locator showed the most promising results, followed by digital radiography and conventional radiography [84].

14.8.2 Ultrasonic Instrumentation

Ultrasonic appliances produce high-frequency vibrations of over 30,000 Hz, which provide better cleaning and smear layer removal inside the canals [86, 87]. The use of K-type files with the ultrasonic technique does not eliminate the need for conventional hand instrumentation [87], so the technique combines manual root canal preparation with sodium hypochlorite 1% or 3% irrigant and K-type files. When the working length is determined, the same file size (usually 15) is used with the ultrasonic technique to enlarge the canals under constant irrigation [43, 86, 87]. The use of ultrasonic instrumentation in primary molars reduced appointment time and showed a high success rate [87] of 97.5%, with a mean follow-up time of 19.9 months [86]. No significant difference in radiographic healing of apical periodontitis was found between ultrasonic and syringe irrigation [88].

14.8.3 Lesion Sterilization Tissue Repair (LSTR)

A new biologic approach in the treatment of carious lesions with or without pulpal and periapical involvement developed at the Cariology Research Unit of the Niigata University, School of Dentistry in Japan, advocates the concept of "no instrumentation endodontic treatment" (NIET). It is also called "lesion sterilization and tissue repair" (LSTR). LSTR procedure for necrotic primary teeth usually requires no instrumentation or filling of the root canals. Instead, an antibiotic mixture is placed in the pulp chamber to disinfect the root canals [25, 26]. For teeth without

preoperative root resorption pulpectomy was more successful than LSTR, indicating it should be preferred over LSTR in these teeth [26].

LSTR procedure: After opening the pulpal chamber of a necrotic tooth, the canal orifices are enlarged using a large round bur to create medication holder. The walls of the chamber are cleaned with phosphoric acid and then rinsed and dried [89]. The 3 Mix-MP [90], an antibiotic mixture of clindamycin, metronidazole, and ciprofloxacin, from crushed tablets, is mixed with a liquid consisting of polyethylene glycol and macrogol to form a paste placed directly into the medication receptacles and over the pulpal floor [89]. It is then covered with a glass-ionomer cement and restored with a stainless steel crown [89]. Following treatment, pretreatment clinical signs and symptoms should resolve, and the radiographic picture of the lesion should show the repair.

The antibiotic mixture targets both aerobic and anaerobic bacteria and sterilizes infected necrotic pulp and root dentine [91, 92]. Similar success rates have been reported for minocycline and clindamycin [93], while tetracycline reduces the success of the mixture [25]. Therefore, the AAPD's practices on the use of non-vital pulp therapies in primary teeth recommend that antibiotic mixtures used in LSTR should not include tetracycline/minocycline and that clinicians replace it with another antibiotic such as clindamycin [26]. Clinicians must consider the fact that the efficacy of antimicrobial filling pastes containing antibiotics decreases over time due to the high prevalence of resistant bacteria in the root canals [94].

The clinician's choice between pulpectomy and LSTR should be based on the following considerations: rate of root resorption, time to exfoliation, and strategic tooth position in the arch. LSTR can be considered effective for teeth with advanced root resorption when conventional endodontic treatment is contraindicated [91].

For teeth without preoperative root resorption, pulpectomy showed higher success rates than LSTR [95, 96]. Based on 12-month results, pulpectomy is preferred over lesion sterilization tissue repair in non-vital teeth with no root resorption. LSTR is preferred over pulpectomy in non-vital teeth with root resorption when a tooth needs to be maintained in the arch for 12 months or less [29].

LSTR-treated teeth did not resorb, unlike untreated contralateral teeth [97]. This treatment adversely affected the permanent tooth eruption due to interradicular bone loss surrounding the crown and, in one case, caused an odontogenic keratocyst [97].

14.9 Evaluation of Pulpectomy

Failure of a pulp treatment is manifested by at least one of the following outcomes: soft tissue pathology, pain, pathologic mobility, pathologic radiolucency, and/or pathologic root resorption [28].

Pulpectomy is considered successful if pre-treatment clinical signs and symptoms resolve within a few weeks. The treated tooth should be painless, with no increased mobility, no sensitivity to percussion, and healthy surrounding soft

tissues. Radiographically, there should be evidence of successful root canal filling without gross overextension [24, 58–60]. The treatment must allow concurrent resorption of the primary tooth root and filling material to permit normal eruption of the succedaneous tooth.

Radiographic findings of lesions pre-treatment should resolve within 6 months, with evidence of bone deposition and a decrease or disappearance [66, 96] or at least no increase in the size of prior radiolucent areas. A static or unchanged radiolucency means the infection is still present but not causing clinical symptoms. Preoperative periradicular radiolucency decreases treatment success and tooth survival following pulpectomy [98, 99].

Cases where pre-existing radiolucent defects have grown or new defects appeared are considered a failure of treatment. No pathologic root resorption, furcation/apical radiolucency [60, 100], or new lesion should appear after treatment.

Clinicians should evaluate non-vital pulp treatments for success and adverse events clinically and radiographically at least every 12 months.

Success rates of root canal treatments in primary teeth have been extensively discussed in the literature, with pulpectomies being generally more successful than pulpotomies [24]. For non-vital teeth, pulpectomy is recommended for long-term success (greater than 24 months) in teeth when there is no root resorption present.

Pulpectomies success varied according to the root canal filling material used and evaluation type (clinical or radiographic): in clinical trials, ZOE had 82–100% success, calcium hydroxide with iodoform pastes had 80–100% success, and iodoform pastes had 93.3–100%. In radiographic examinations, ZOE had 65–100% success [55, 60, 64, 66, 74, 96, 100], calcium hydroxide had 72.5–100%, and iodoform pastes had 72.5–90.3% success [24]. A review of clinical and radiographic follow-ups up to 24 months did not find sufficient evidence to establish the superiority of one medicament over another regarding clinical failure [101].

Another factor of pulpectomy success is the follow-up period. For long-term success (greater than 18 months), ZOE/iodoform/calcium hydroxide or ZOE fillers perform better than iodoform fillers [29]. Endoflas and zinc oxide eugenol showed 93.3% success, whereas a higher percentage of success was observed with Metapex (100%) [69].

ZOE with iodoform, calcium hydroxide with iodoform, and ZOE were found to have more than 90% success rate and were all equally effective at 30 months [56].

Restoration time: Data of 24-month follow-up suggests that teeth restored with stainless steel crowns had better success than composites (90% vs. 77%). Success rates for 1 year posttreatment did not differ between restorations placed on the same appointment as the pulpectomy and restorations placed at the next appointment (82% compared to 83%) [26].

Obturation method, number of treatment visits, method of root length determination, irrigation solutions, smear layer removal, timing/type of the final restoration, and type of tooth treated (molar versus incisor) do not impact the success rate of pulpectomies [29].

14.10 Adverse Effects of Pulpectomy

Little is known about the consequences of primary teeth pulpectomy on the development of permanent tooth buds and the eruption of the permanent teeth.

The type of root canal filling material, preoperative periapical radiolucency, and inadequate treatments have been shown to influence pulpectomy adverse effects.

Type of root canal filling material: ZOE filling material has a 20% chance of altering the path of permanent tooth eruption [57]. ZOE tends to resorb more slowly than the root of the primary tooth and may be retained after pulpectomized tooth exfoliation. Remnants of ZOE were found in the alveolar bone of up to 70% of exfoliated primary teeth, and the material was still retained in more than a quarter of the patients 3 years posttreatment [102, 103]. Retained ZOE may deflect the permanent tooth's path of eruption [52].

In the case of traumatized incisors that had a pulpectomy, ectopic eruption of a permanent incisor might also be due to the trauma to the primary incisor affecting and/or dislodging the developing permanent bud. Incisor pulpectomy success rates do not appear to be much different if treated due to trauma or caries after 12 months [29].

Contrary to ZOE, iodoform fillers resorb at a *faster* rate than the root, resulting in the pulpectomy filling looking more like a pulpotomy after 12 to 18 months [57, 99, 102]. Also, iodoform-containing root canal filling was found to accelerate root resorption [104].

Leakage of root canal filling material from resorbed primary apices might lead to low-grade irritation to the dental sac of the permanent successor and to development of radicular cysts around the permanent tooth buds [99, 105]. Enlargement of the dental sac in association with a root treated primary tooth occurred in 3.3% of the followed cases, but the development of a true radicular or dentigerous cysts was rare. Despite the low occurrence, dentists should be aware of this phenomenon and radiographically monitor root canal treated teeth until shedding [105]. Most radicular cysts in the primary dentition do not demonstrate clinical signs, but cysts of a certain size might displace the developing tooth bud [16, 57, 106, 107] and expand the buccal cortical plate [16, 107].

Although rare, hypoplasia in the permanent successor as a sequela to a pulpectomy in a primary tooth may occur even after a successful pulpectomy [99, 108].

Incorrectly performed root canal treatments may stop the eruption of the succedaneous teeth [109]. Canal overfilling may cause a mild foreign-body reaction and an increased failure rate when compared to underfilling or flush finishing [74].

14.11 Adjunctive Systemic Antibiotic Treatment

Dentists prescribe approximately 10% of antibiotics dispensed in primary care and so contribute to the development of antibiotic-resistant bacteria [110]. In root canal treatments, the lack of blood circulation in the root canal prevents antibiotics from

reaching the area and renders them ineffective in eliminating the microorganisms [111]. The American Association of Endodontics guidelines [112] stress that the most important step in the treatment is dental management of the condition or referral for endodontic management of the patient. Systemic antibiotic treatment in conjunction with endodontic therapy is indicated in the following cases:

1. Acute apical abscess in medically compromised patients.
2. Acute apical abscess with systemic involvement, e.g., localized fluctuant swellings, elevated body temperature, malaise, lymphadenopathy, and trismus.
3. Progressive infections (rapid onset of severe infection over less than 24 h, cellulitis or spreading infection, osteomyelitis).
4. A systemic antibiotic is **not** indicated in the following:
   (a) Symptomatic irreversible pulpitis (pain, with no other symptoms and signs of infection).
   (b) Pulp necrosis.
   (c) Symptomatic apical periodontitis (pain, pain to percussion and biting and widening of periodontal ligament space).
   (d) Chronic apical abscess (teeth with sinus tract and periapical radiolucency).
   (e) Acute apical abscess without systemic involvement [113].

Antibiotics should be prescribed only when genuinely needed and only as an adjunct to, not an alternative to, other interventions (e.g., pulp therapy or extraction) to control the infection source [114].

Amoxicillin is the drug of choice for dental infections in non-allergic children. It has been shown to be effective against oral flora; is well absorbed from the gastrointestinal tract; provides high, sustained serum concentrations; and has a low incidence of adverse effects [114]. Moderate to severe pain 24 h post a pulpectomy procedure is rare [29], and it is important to note that antibiotics do not affect pain associated with dentoalveolar infection [115]. The use of antibiotics before endodontic treatment of asymptomatic non-vital teeth has no effect on the flare-up rate [115].

The traditional minimal duration of a drug regimen is 5 days beyond the point of substantial improvement. Patients' compliance with the treatment can be improved by prescribing medications that can be given once or twice daily rather than three times a day. For odontogenic infections with non-localized and progressive swelling and systemic manifestations (e.g., fever, difficulty breathing or swallowing), immediate surgical intervention and medical management with intravenous antibiotic therapy expedite the cure.

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Sealing and Building Up the Pulp Chamber and Crown with Glass Ionomer and Other Materials After Pulp Therapy

15

Joel H. Berg

Contents

15.1 Introduction

This chapter will discuss the ever-important component of pulp therapy that includes the filling of the pulp chamber after completion of the pulp therapy per se and prior to the external restoration of the tooth. Although this content is discussed discreetly, it overlaps with other topics discussed in other chapters in this book. The materials that will be discussed in this chapter as well as the techniques of using those materials may also be discussed in the context of other aspects/chapters of this book, yet herewith we will discuss the specific use of these materials and techniques for the purpose of pulp chamber filling.

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15.2 Premise and Conceptual Framework

When one considers the various aspects of pulp therapy for children, filling of the pulp chamber is a very small component. However, structurally and from the perspective of sealing is an extremely important part of the overall process. Therefore, although this chapter is shorter in length than many of the other chapters in this book, it provides connectivity to the other components of the pulp therapy process from the just completed pulp therapy below, as well as sealing the tooth structure so that the restorative material placed above the pulp chamber fill is intact and protected against further destruction.

In terms of structural integrity of the tooth, one can imagine that by removing tooth structure to gain access to the pulp as part of the pulp therapy process, there may be enough destruction/removal of tooth structure to allow degradation of the quality of the strength of the crown of the tooth regardless of subsequent restoration. For permanent teeth, and for crowns or other, the crown buildup procedure is a common part of the process. In fact, it is deemed to be a separate procedure with its own procedure code and own billing components. Generally speaking, most crowns for permanent teeth regardless of how they are restored are preceded by the placement of a so-called crown buildup procedure. This procedure discussed over many decades has evolved into what results in the preparation of the tooth prior to receiving the external restoration. In other words, for permanent teeth, after the buildup, the final restoration of the tooth structure can be placed so that it can receive an extracoronal restoration such as a full crown [1–4].

In the case of primary teeth which have received pulp therapy, the situation is a little bit different. First, the volume of tooth structure removed to gain access through the pulp chamber into the pulp area where the procedure is performed is much smaller [5]. Therefore, the relative strength loss in terms of structural integrity of the tooth is reduced significantly from what it would be in a permanent tooth [6, 7]. Even though there may be a high percentage of volume removed to gain access to the pulp in order to perform the pulp therapy in the case of a primary molar, it is adequate to preserve the original strength of the tooth and to ultimately receive a restoration above, be it in intracoronal or extracoronal [8–12].

Regarding sealing, let us first discuss sealing above the orifices that have been previously sealed as part of the pulp therapy procedure. For purposes of our discussion in this chapter, we will assume that the pulp therapy has been completed per instructions as discussed in other chapters. For example, the pulp therapy was completed with removal of the vital or nonvital tooth structure, cleaning and drying, and filling of the pulp chamber where the pulp resided previously; the orifices must have been sealed at the conclusion of that procedure. This usually takes place together with the component of the procedure we are now discussing. We will discuss them as discrete procedures. Therefore, I will not go into detail on the pulp therapy per se as discussed in detail in many other chapters but will discuss solely the filling between the sealing of the pulpal orifices and the external restoration of the tooth. With the assumption that the pulp therapy is completed, and the orifices have been sealed with mineral trioxide aggregate (MTA), we now must guarantee that the seal

is continued into the pulp chamber and then externally to the restoration which is placed above the pulp chamber fill [13–18].

This is easily achieved with a variety of materials. We will discuss a few of them in this chapter and why those materials are the correct materials to be used in this circumstance, that is, filling of the pulp chamber itself. Our definition of pulp chamber for purposes of this component of the procedure is that component of the tooth structure was removed to eliminate decay or to gain access to the pulp itself in order to perform the pulp therapy procedure.

15.3 Boundaries of This Chapter Conversation

After pulp therapy and sealing the orifices (this chapter will discuss the proper methods of guaranteeing a seal over the orifices, as well as the proper choice of material), the actual build-up of the pulp chamber cavity to fill the chamber created by removing decayed tooth structure or healthy tooth structure in order to access the pulp for the pulp therapy procedure must be completed.

As an extrapolation from the science of permanent tooth root canal therapy, Gillen et al. [19] performed a critical systematic review examining the factors important to the successful outcome of RCT in permanent teeth. It was concluded that more important than the method of root canal treatment or fill technique were two elements. The seal of pulp treatment from above, the seal of the ultimate restoration of the tooth [19]. "On the basis of the current best available evidence, the odds for healing of apical periodontitis increase with both adequate root canal treatment and adequate restorative treatment. Although poorer clinical outcomes may be expected with adequate root filling-inadequate coronal restoration and inadequate root filling-adequate coronal restoration, there is no significant difference in the odds of healing between these two combinations" [19].

Although there is inadequate literature regarding the impact of these same factors on the success of primary tooth pulp therapy with the same level of evidence, there is reason to believe from the existing literature, as discussed on other chapters of this textbook that the same biological principles apply [20–28].

15.4 Purpose of Fill/Goals

The restoration of choice for primary molars following pulpotomy has traditionally been the stainless-steel crown; this extracoronal restoration requires the removal of tooth structure beyond that affected by the decay and the pulpotomy procedure. Although this chapter will not discuss the ultimate restoration of the tooth after pulp therapy, it will discuss the buildup of the core opening to access the pulp chamber in order to perform pulp therapy.

Over the last decades, various materials have been formulated to fill the pulp chamber after sealing the pulp orifices after completion of a pulpotomy. The most common material has been the use of zinc oxide eugenol (ZOE), as a paste to seal

the orifices of the pulp chamber and also to fill the pulp chamber entirely up to the point of the ultimate restoration whether it be a stainless-steel crown or other type of material [29–34].

This author reported on the use of glass ionomer combined with silver material as an ideal choice of material to fill the cavity of the pulp chamber created by access in order to perform pulp therapy material which provides all the properties of a traditional glass nominator with the additional strength characteristics of silver [35–39]. Today, modern glass ionomer materials are quite useful for this purpose, as they are strong and also yield incredible sealing characteristics, being that glass ionomer materials are the only material which chemically bonds to structure, thereby applying a seal. Any other choice of material requires an intermediate bonding step above pulp chamber orifices in order to provide an effective seal.

15.5 Sealing the Orifices

Mineral trioxide aggregate (MTA) has been clearly documented to be the material of choice to seal the orifices and to complete a primary molar pulpotomy procedure. In a search of the literature over nearly 20 years of work, Musale et al. showed that the use of MTA as a sealing agent during and after primary tooth pulpotomy was evaluated to be extremely successful. "MTA pulpotomy has been a successful treatment modality in primary molars with proven success over the years" [28]. The procedure for performing a pulpotomy using MTA as the pulp orifice sealing agent during and after the completion of the pulp therapy itself is discussed in other components of this textbook.

Having completed the pulp therapy using MTA, it is now important to direct our attention to providing "contiguity of seal" within and above the orifices of the now sealed pulp therapy. This provision of seal integrity is provided by the use of appropriate materials for filling the access area created by performing the pulp therapy procedure [40–46].

15.6 Material Choices for Pulp Chamber Fill

15.6.1 Zinc Oxide: Eugenol

Historically, a variety of materials have been used to fill the pulp chamber after a pulpotomy procedure. Namely, zinc oxide eugenol (ZOE) combination cement materials have been employed with great prevalence of use. Although these materials provide some kind of interface and meet the objectives of filling the pulp chamber access area, they are not ideal for creating a contiguity of seal and similarly are not ideal for providing structural strength for the tooth. Therefore, it is not recommended to use ZOE for this purpose [47, 48].

15.6.2 GIC Materials

Glass ionomer has been shown to be a useful and nearly ideal material for filling the pulp chamber after pulp therapy in primary molars [35].

Glass ionomer cement is a salt, by chemical definition, which is formed by the reaction between a polyalkenoic acid and an aluminum-containing glass. Aluminum, as a constituent element in the glass, is critical for the glass ionomer reaction to occur. Most commonly, the "base" part of the reaction is the glass. Water is a necessary ingredient of glass ionomer, as an acid-base reaction can only occur in a water-containing medium. Fluoride is added to the glass material and is released over time to provide additional benefit to the material. This describes a so-called traditional glass ionomer material. Modern materials often contain resin mixed with the glass ionomer to allow a "resin-modified" glass ionomer material to be used. Such materials are denser in composition, have improved mechanical properties offering more significant strength, and are less brittle due to the resin additives [48, 49]. Glass ionomer can be used as a liner, as luting cement, as a base core material, such as we are discussing herewith, and as a restorative material. As a pulp chamber filling material, glass ionomer acts as a restorative material to restore the pulp chamber component of the tooth, which was destroyed during access to provide the pulp therapy. Glass ionomer offers the advantage of being the only material used in dentistry with a true covalent chemical bond with tooth structure.

Therefore, (most effectively with MTA) there is a seal between the glass ionomer and not only with the MTA material itself, but to even a greater extent with the surrounding dentin and enamel that were hollowed out during the access to perform the pulp therapy procedure. Even though the measured in vitro bond strength of glass ionomer to tooth structure is lower than the bond strengths of other materials such as resin composite, experience shows that glass ionomers are very well retained. This is due to the fact that the chemical bond has a different character than the purely mechanical bond of other materials, such as resin composite. Certainly, within the pulp chamber, glass ionomer is particularly well suited, as the otherwise present shear and compressive forces that might be destructive to a restoration made of this material are not exhibited or manifested within the pulp chamber, which is subsequently covered with an alternative form of ultimate restoration such as with a stainless-steel crown or a resin composite material above.

As mentioned, physical properties of traditional glass ionomers have been improved recently with the introduction of high powder-to-liquid ratio glass ionomer materials. These denser materials, although not containing monomeric resin, are stronger and provide a "condensable" feel, facilitating placement into pulp chambers. These strong materials have improved compressive and flexural strengths, allowing their use (without resin) to be sustainable pulp chamber filling materials [50, 51], when used as a buildup material after primary tooth pulp therapy. Another advantage of glass ionomer materials, compared with essentially every other material that has been used to fill the pulp chamber, is the compatible coefficient of thermal expansion. Glass ionomers have a coefficient of thermal expansion quite similar to dentin. This compatibility means that as the tooth naturally expands and

contracts with variations in temperature during eating and drinking foods of various temperatures. The mere continuous presence of saliva in the mouth will not subject the glass ionomer material or the tooth to fracture as a result of incompatible expansion characteristics.

Recently, in discussing the best materials for pulp chamber filling, glass ionomers continue to be recommended particularly to be used to fill the pulp chamber. One potential disadvantage of course is because these materials are self-curing it can take several minutes for them to fully harden (actually full setting might take as long as 24 h, with the initial stability after 5–7 min). However, as part of the pulp therapy procedure when the pulp chamber is filled in this instance with glass ionomer, be at resin-modified or otherwise, by the time the restoration is immediately placed above (whether it's a stainless crown or a resin composite), the glass ionomer will be fully set even if it's in its pure form, by the time the full procedure is completed. Some clinicians prefer to use resin-modified glass ionomer because of their handling characteristics. They are less sticky, where stickiness can be the case with traditional glass monomers.

The resin-modified glass ionomers also possess command cure characteristics. However, the cure of the glass ionomer itself, that is, the acid-base reaction, only takes place after several minutes and is fully set within 24 h. This further makes either traditional glass ionomers or resin-modified glass monomers, highly suited to the to be used as a pulp chamber filling material.

15.6.3 Composite

Composite resin, also known as resin composite, is the most esthetically desirable material in terms of filling materials for pediatric or adult dentistry. Composite resin contains a monomeric or pre-polymeric resin that is filled to various levels with glass or quartz. The filler particles are silanized to allow the hydrophilic filler to bond to the hydrophobic resin material. As a result, this resin composite material ends up being quite hydrophobic, and there must be an intermediate bonding layer placed to allow it to bond to the tooth structure mechanically.

Although the bond is strong as a mechanical bond, the material requires several additional steps in the etching, priming, and bonding to obtain an acceptable bond between the composite material and into the structure. In the instance of pulp chamber filling, the advantage of resin composite is that it is quite strong for filling, an important objective toward structural integrity of the tooth. If the ultimate restoration of the tooth above is to be made with resin composite, then composite within the chamber could be a contiguous component of the restorative material above, as opposed to a separate component [51].

However, it can be argued that the composite in this instance is less desirable than it might be as an intracoronal restoration. Additionally, because the coefficient of thermal expansion of resin composite is not compatible with dentin, it is more challenging as a pulp chamber filling agent than glass ionomer alone, which itself is an adhesive. One must also be aware that the polymerization shrinkage of

composite can be significant, making it less suitable than glass ionomers which do not undergo significant polymerization shrinkage. Resin composite could shrink as much as 2 or 3% which alone could cause fracture or leakage problems later once the ultimate restoration is placed.

As with any clinical situation evaluating which material should be used for a given situation must include a determination of the *in situ* characteristics after the restoration is placed. Therefore, when one weighs the advantages and disadvantages of the various materials which might be used to fill the pulp chamber after completion of pulp therapy in primary teeth, it becomes quite clear that the use of glass ionomers is particularly suitable for this circumstance. Although we could list a multitude of other materials that might be used to fill the pulp chamber, and indeed many have been used over many decades, today with the expansive development of glass ionomers as they are, it seems that this is the most suitable material to fill the pulp chamber component. In some instances, where the orifices of the primary molar are well covered with MTA, and there exists only a small "pulp chamber" space below the ultimate restoration using a stainless-steel crown, perhaps in this instance the MTA alone would be sufficient to fill the pulp chamber and an intermediary layer of glass ionomer might not be necessary or purposeful.

15.7 Assessment/Outcomes

Going back to what was stated throughout the chapter, it is always important to have situational awareness. This means being attentive to the exact nature of the tooth structure situation, what is remaining, what has been removed, and what needs to be restored. Once this awareness is in place in the mind of the clinician, only then can the suitable materials and methods be deployed correctly. One must situate themselves in the clinical circumstance present at the time and be certain that after placement of all aspects of the restoration, having completed pulp therapy on a tooth, what is best suited to sustain the tooth in the mouth in a healthy fashion, until the natural exfoliation of the primary tooth. As it turns out, this very small aspect of the overall treatment, the filling of the pulp chamber, is a major determinant of success of the overall pulp therapy procedure.

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Restorative Guidelines for Endodontically Treated Primary Teeth

16

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16.1 Introduction

The ideal dental restoration should replace and maintain the integrity of tooth structure and the dental arch from a growth and development perspective. It should seal the restoration from the oral environment, decreasing the susceptibility to recurrent lesions and infection. Material selection and quality of the restoration are paramount to ensure tooth and restoration longevity [1].

A variety of restorative materials are available. Once the clinician understands materials' properties and indications, the selection should be based on individual needs [2]. However, multiple factors must be taken into consideration regarding the patient and the provider: caries risk, age and behavior, remaining tooth structure, tooth type (anterior versus posterior), longevity of the tooth, esthetics, clinical skills, practice limitations and resources (academic, private, public health, military, corporate), and financial considerations [3].

After accurate diagnosis and treatment of the pulp, quality restorative work is imperative for pulp treatment success. Failures may be due to non-ideal restorative choices, poorly placed restorations, or temporary restorative treatment that never received a definitive restoration and ultimately failed. Parents' demand for esthetics is a key factor in contemporary pediatric dental practice. When integrating pulp therapy into the highest esthetic result, it is imperative to only use non-staining pulp medicaments and avoid leaving silver diamine fluoride (SDF) as part of an indirect pulp cap (IPC) treatment as both agents may result in dark tooth-colored restorations, dark strip crowns, and dark zirconia crowns.

The periapical radiograph below (Fig. 16.1) is an example of a young child who received two pulpotomies with mineral trioxide aggregate (MTA) on teeth K (75) and L (74) and stainless-steel crowns. Failed treatment in this case could be attributed to poor diagnosis of the pulp treatment needed, inadequate mix of MTA in combination with inappropriate packing of the MTA that did not make adequate contact and failed to seal the pulp stumps. Moreover, the oversized crowns may have led to washout of the cement and ultimately the MTA, rendering bacterial penetration into the pulp causing abscesses. Without excellent pulpal medicament contact with the pulp to promote healing and seal with a competent restoration, pulp treatment will most likely be compromised.

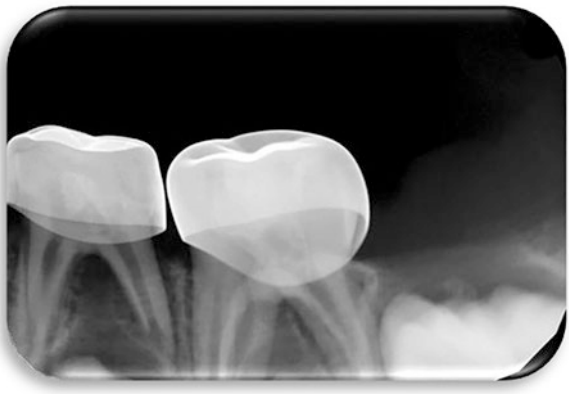

Fig. 16.1 Symptomatic teeth after failed MTA pulpotomies on teeth # K (75) and L (74) restored with stainless-steel crowns

For primary anterior teeth, full coronal restorations are recommended when multiple surfaces and/or the incisal edge are involved and after pulp therapy. The options available are resin-based bonded restorations (strip crowns), co-polyester crowns, metal-based esthetic crowns (composite resin placed on open-faced stainless-steel crowns, pre-veneered stainless-steel crowns), and zirconia crowns [4]. Examples, indications, and contraindications for each of these crowns are illustrated throughout this chapter, with the exception of co-polyester and open-faced stainless-steel crowns, as they are no longer considered the standard of care. Posterior tooth full coronal coverage options include stainless-steel crowns, zirconia crowns, and the latest contempory option, high strength resin polymer crowns. In limited situations after pulp treatment, amalgam and composite resin restorations may be considered (Refs- Image of reference at the end of the chapter) [5]. The goal of this chapter is to provide clinicians with guidance and options for restorative procedures on endodontically treated primary teeth considering the aforementioned factors.

16.2 Beyond the Tooth… Patient Behavior, Clinical Skills, Modality of Care Delivered, and Special Healthcare Needs

Prior to initiating any treatment, providers must complete a thorough review of medical history; decide the best modality of treatment whether it be conventional with or without nitrous oxide, conscious sedation, or general anesthesia; and provide local anesthetic when indicated. Providers may also consider ibuprofen (acetaminophen if kidney problems, bleeding issues, taking lithium, ibuprofen is contraindicated with other medications taken, other medical issues that may contraindicate ibuprofen, or allergy to ibuprofen) 30 min prior to treatment to reduce inflammation and the onset of sensitivity when local anesthesia becomes ineffective (anesthesia disassociation discomfort).

Dentistry is an art. Each clinician comes with his/her set of strengths and challenges. This combined with the uniqueness of each patient needing treatment creates a labyrinth of options to navigate to make the best restorative recommendation. Some restorations are more technique-sensitive, requiring a more cooperative patient and seasoned clinician for success. For example, strip crowns, class II and III tooth-colored restorations, and zirconia crowns (particularly posterior and back-to-back with space loss and crowding) require advanced behavioral coaching and clinical skill mastery to treat conventionally. Alternately, class I composites, amalgams, and stainless-steel crowns (all not as technique-sensitive) usually may be successfully accomplished despite behavior and clinical experience.

Many clinicians do not venture beyond their training in their practice restorative options. For example, despite being proven to be inferior to pre-veneered or zirconia crowns in long-term parent satisfaction, many clinicians only place strip crowns as this was the preferred choice restoration their faculty taught for anterior esthetic crowns in primary teeth [6].

Finally, beyond the tooth, the modality of delivery of treatment chosen often dictates treatment options given to parents. The literature states that long-term

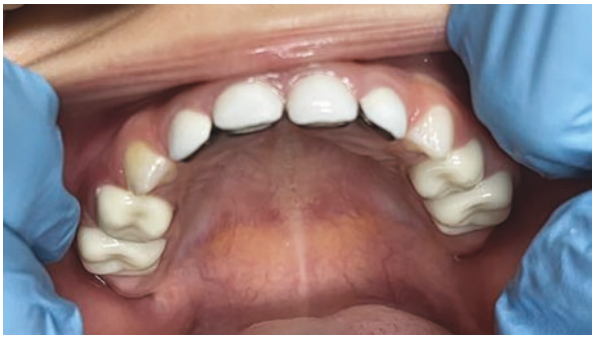

Fig. 16.2 Zirconia crowns placed on primary molars and pre-veneered stainless steel crowns on primary incisors

clinical success of full coronal coverage is more predictable than fillings for young children treated in the operating room under general anesthesia [1].

Providers must be mindful to not predetermine care based on the patient's socioeconomic status, their training, and/or their preferred treatment to deliver. From a legal standpoint, it is the responsibility of each provider to educate parents of all restorative options and modality of delivery of care available for their children, whether they provide these services or need to refer to a provider who routinely provides these services. The patient below (Fig. 16.2) was treated with nitrous oxide in office. Multiple teeth required pulp therapy and the parent chose to place zirconia crowns on the posterior teeth (that the insurance did not cover) and pre-veneered crowns on the anterior teeth (that insurance did cover) to save money due to the understanding the posterior teeth would be present significantly longer than the anterior teeth.

Patients requiring space maintenance may still choose zirconia crowns despite knowing a metal band will be placed with the forward thinking of the band being removed in the future. Clinicians must ensure parents understand if zirconia crowns oppose stainless steel crowns, the zirconia will develop dark spots where the zirconia occludes with stainless steel. These may easily be polished away; however, they will return as long as the zirconia crown occludes with stainless steel (Fig. 16.3) [7].

Patients with special healthcare needs may require advanced imaging of the head and neck area for various non-dental medical reasons. In these situations, a provider must ensure their pediatric dental care does not compromise the diagnostic quality of the imaging, particularly with magnetic resonance imaging (MRI). For example, zirconia does not create artifact whereas stainless-steel crowns create significant artifact [8]. A good option for providers not comfortable with zirconia crowns restoring pulpally treated teeth on a child requiring MRI are large composites with orthodontic bands placed over for extracoronal support and protection that may be removed when an MRI is needed.

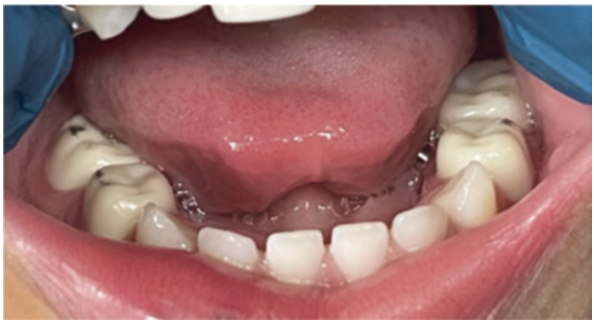

Fig. 16.3 Marks on zirconia crowns when in occlusion with stainless steel crowns

16.3 Isolation

Pulpal and restorative treatment success is enhanced with quality isolation. Rubber dam isolation (RDI) remains the highest standard in isolation for pulp treatment and restorative treatment in addition to the best infection control barrier from communicable microbes such as the coronavirus. Rubber dam isolation is a fraction of the cost of Isolyte®-type devices and provides the best consistent posterior depth of field due to rubber dam clamp design. Retraction and protection of the soft tissue, and view for the doctor and assistant are also superior with RDI. When using clamps with wings placed in tandem with the rubber dam proper (advanced technique), triggering the gag reflex can also be avoided or lessoned. The only downside to RDI is that for the completion of a prep and final fit and cementation of a crown on the most terminal erupted tooth being treated in a sequence, the rubber dam must be removed. It is not uncommon for providers trained since Isolyte®/Isodry®/Isovac®-type technology has arisen to not become proficient in placing and training dental auxiliary to place a rubber dam. There are myths that the placement of a rubber dam is less efficient or more difficult for an anesthetized patient. Once placement is mastered, RDI provides equally efficient isolation to Isodry®-type devices with equally compassionate placement. Below are enhancements to simple RDI to further increase efficiency and meticulous isolation. The two rubber dam clamp technique for half-mouth isolation offers providers the ability to prep teeth with a high speed handpiece, remove caries with a slow speed handpiece, treat the pulp, and restore two quadrants at one time (Fig. 16.4). With younger children requiring treatment of first permanent molars, sometimes space does not allow simultaneous isolation of both upper and lower quadrants. It is also common when treating children conventionally (no sedation nor general anesthesia) to only complete treatment in one quadrant.

Primary canines and incisors have ideal morphology with a well-defined constriction at the cemento-enamel junction to place floss ligatures to enhance isolation for restoration success. The child shown below (Fig. 16.5a, b) had deep lingual caries and received indirect pulp treatment. This child was treated in office with local anesthetic, nitrous oxide, and oxygen and is an acceptable candidate for composite resin restorations. This is due to evidence of compliance noted by further eruption

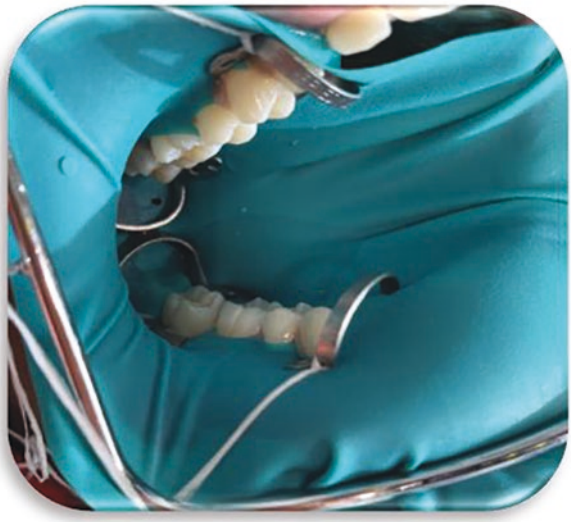

Fig. 16.4 Rubber dam isolation technique for half-mouth approach increasing efficiency

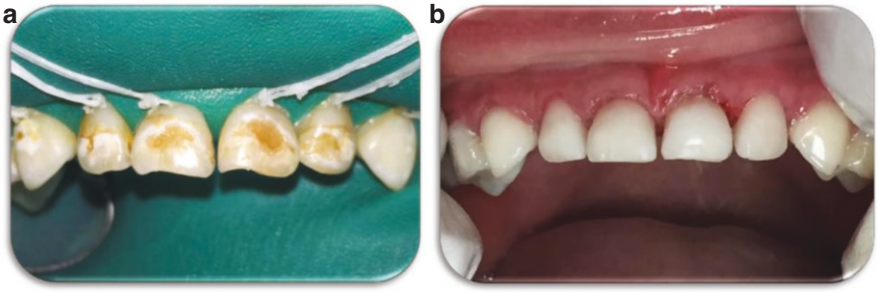

Fig. 16.5 (**a**) Preoperative maxillary incisors and canines with deep lingual caries ready to be restored with composite resin restorations. (**b**) Immediate postoperative outcome

of teeth without continued cervical demineralization, lack of caries on the incisal edges, and conventional treatment (versus requiring general anesthesia where full coronal coverage offers a more predictable long-term restorative outcome to avoid future general anesthesia encounters).

The best indication for Isolyte® isolation is for sealant placement when local anesthetic is not required (may still need the operculum gently retracted with a PF1 as shown below Fig. 16.6).

An additional benefit of Isolyte® is the ability to complete the preparation of the distal aspect of the most terminal erupted tooth in the arch without removal prior to crown cementation. However, providers must understand these devices in comparison to RDI limit handpiece maneuverability, dental assistant visibility, and also

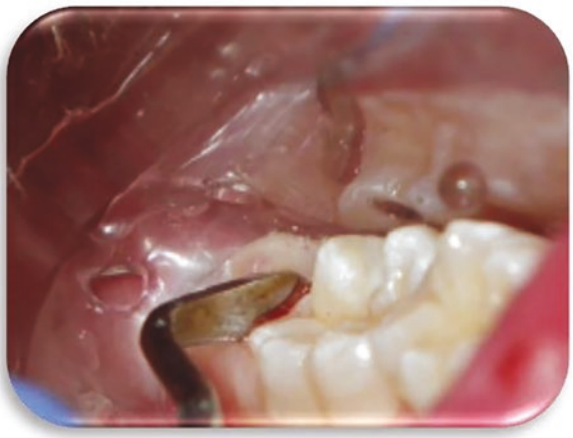

Fig. 16.6 Isolyte® system isolation facilitating sealant placement on a partially erupted first permanent molar with PF1 retraction of operculum

increase expense. Additionally, not all children can tolerate these devices. In these cases, the gag reflex, movement, and hypersalivation may compromise restorative quality (nitrous oxide may help suppress the gag reflex).

16.4 Mouth Props and Bite Blocks

For safety, a mouth prop or bite block is recommended for children during local anesthesia and restorative treatment (Fig. 16.7). For young children, the Molt type mouth props are the standard. Another variation of the Molt type mouth prop is the Denhardt mouth prop. The Denhardt is ideal for use when restoring anterior teeth. The downside is that the lack of silicon sleeve makes it potentially uncomfortable for children with shallow vestibules (shown Fig. 16.13c). Caution should be used to ensure the lips and lingual frenum are free from impingement when using any Molt type mouth prop, particularly in a child who has a numb lip or lips. In addition, the provider must be cognoscente to ensure the silicon protective tubes do not slide off and pose an airway issue.

A benefit of the Isolyte®-type isolation is the built-in mouth prop. Bite blocks are more frequently used in teenagers or with children under conscious sedation or general anesthesia where positioning is less contingent upon cooperation.

Fig. 16.7 Molt type mouth prop to maintain mouth opening

16.5 Amalgam Restorations

Amalgam has a history of scrutiny and is not allowed in some countries, while in others it is still permitted and readily used. It possesses qualities favorable for restoring primary teeth with limited loss of tooth structure during indirect pup capping. Unlike composites, amalgam restorations' seal may increase over time, increasing their longevity [9].

Prepping keys	Common errors	Placement
Remove all caries/organic material and/or affected hard tissue for caries and/or moderate to severe enamel hypomineralization (affected, even if non-carious, demineralized tissue will be an area susceptible to new caries if hygiene, diet, and availability to fluoride are not ideal). The exception is a plan to treat with an indirect pulp cap where caries are deliberately left to avoid pulp exposure. Utilize extension for prevention (enter grooves and ensure the adequate thickness of amalgam is 2mm or more to resist fracture) or seal unaffected grooves with sealant material after amalgam placement. Ensure that no undercuts or unsupported enamel rods are present to avoid enamel fractures.	Inadequate isolation Soft tissue penetration resulting in an amalgam tattoo For class II restorations: • Not dropping the gingival floor adequately (the interproximal box must extend beneath the interproximal contact) often results in recurrent caries at the contact in a high caries risk patient • Incomplete caries removal in the interproximal box • Overhang due to improper band fit, wedge placement, and/or lack of finish • Parent's lack of understanding that the filling would not be tooth colored • Lack of discussion regarding the controversy of amalgam	1. Caries removal/pulp treatment 2. For class II: band system placed with wedging (sometimes 1–3 wedges of varying sizing are needed for optimal band adaptation) 3. Remove unsupported enamel rods at margin of the gingival floor and band with an explorer or enamel hatchet 4. Triturate, pack, burnish, and carve amalgam 5. Check occlusion 6. Post-op polishing has lost popularity due to knowledge that warming the restoration may release mercury vapor

16.6 Composite Resin and Compomer Restorations

Class I restorations may be utilized after IPC or, in rare situations, a pulpotomy with a plan to place an orthodontic band over the restoration to enhance tooth resistance to fracture. In that situation, a glass ionomer cement layer is needed to prevent inhibited polymerization (when utilizing eugenol-containing products) or washout of pulpal medicament. If the decision is made to place a composite in a tooth requiring pulp treatment, enough tooth structure must be available to serve the patient until exfoliation [10].

The images below are of the pre-op of a tooth treated with an IPC and composite resin restoration, the 1 year post-op, and the 2 year post-op (Fig. 16.8a–c). This example highlights deep caries with adequate tooth structure remaining circumferentially to allow a filling versus a crown. This child had an isolated enamel defect resulting in deep caries in one tooth rather than having poor oral hygiene and dietary habits, a high caries risk, and multiple teeth requiring restorations.

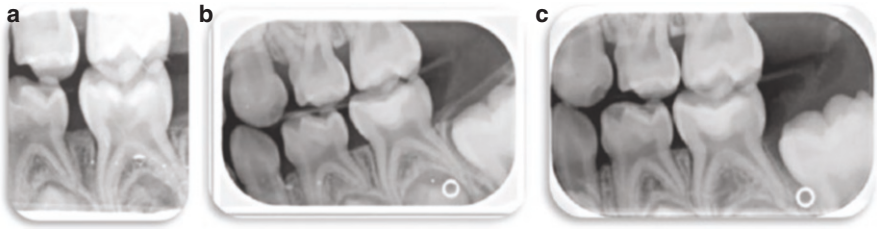

Fig. 16.8 (**a**) Preoperative image showing deep carious lesion affecting the left mandibular second primary molar (**b**) 1-year post-op of MTA IPC and composite restoration (**c**) 2-year post-op of MTA IPC and composite restoration

Prepping keys	Placement
Remove all caries/organic material and/or affected hard tissue by caries and/or moderate to severe enamel hypomineralization. Affected, even if non-carious, demineralized tissue will be an area susceptible to new caries if hygiene, diet, and availability to fluoride are not ideal. The exception is a plan to treat with an indirect pulp cap when caries are deliberately left to avoid pulp exposure.	1. Caries removal/pulp treatment/glass ionomer liner between pulp treatment and composite (if eugenol-based pulp material is used or concern of washout of MTA) 2. For class II: band system placed with wedging (sometimes 1–3 wedges of varying sizing are needed for optimal band adaptation) 3. For class III: utilization of a clear strip and finger adaptation 4. Remove unsupported enamel rods at margin of the gingival floor and band with an explorer or enamel hatchet 5. Wash and dry 6. Etch 30 seconds with 37% phosphoric acid 7. Bond, dissipate bond with air, cure agent 10-20 seconds (if using a standard meter tested curing light) 8. Composite placement: Flowable composite alone is acceptable in limited shallow situations in primary teeth with class I restorations (not acceptable for any restoration over a lesion deep enough to warrant pulp treatment). Packable composite is the standard for composite restorations. It is advisable to place a flowable layer before packable if an extensive lesion is present to reduce pull-back of the packable composite. It is also advisable to place a small amount of flowable in the interproximal box to reduce voids at margins that may not be visualized by the clinician. 9. Polymerization with meter tested curing light or lights from two directions to reduce polymerization shrinkage (that may create sensitivity) if it is a large restoration for 20-40 seconds (if using standard curing light) 10. Depending on the size of the prep, incremental composite curing may be needed and the use of two curing lights is recommended. As a general rule, polymerization during curing is ideal for 2mm; as an example, if you have an occlusal composite 4mm in diameter, a dental assistant and doctor curing from buccal and lingual will create ideal polymerization. This applies to all surfaces. 11. Provider should be mindful of dental assistants polymerizing materials as their view and position may not be as ideal as the doctor and often the light is angled (causing inconsistent intensity) versus perpendicular to the material 12. Finish 13. Re-etch to remove the smear layer from finishing 14. Seal to ensure no micro voids at the cavosurface margin (clear seal for anterior teeth) 15. Check occlusion 16. If extensive tooth structure is removed, and full coronal coverage with a crown is not possible, the placement of an orthodontic band is recommended 17. Perforated metal strips are most efficient to finish the gingival margin of the interproximal box and interproximal contacts. If a caries-free tooth has drifted into the tooth to be restored due to caries, these strips may be useful to create more space in the mesial-distal dimension prior to restoring. Utilize the smooth (nonabrasive) area in the center of the strip to pass through the contact prior to engaging in smoothing the gingival margin of the interproximal box if it is desired to maintain mesial-distal width and an ideal contact is present.
Common errors	
Inadequate isolation For class II restorations resulting in recurrent caries or further demineralization and loss of restoration: • Not dropping gingival floor adequately (the interproximal box must extend beneath the interproximal contact) often results in recurrent caries at the contact in a high caries risk patient • Incomplete caries removal in the interproximal box • Overhang due to improper band fit, wedge placement, and/or lack of finish • Incomplete polymerization in the interproximal box resulting in an incomplete seal and leaking at axial walls and gingival floor margins resulting in recurrent caries Common errors in class III composite restorations: • Relying on wedges to adapt clear strips may notch the interproximal contour of the material and promote gingival hemorrhage. In contrast, finger pressure adaptation of the clear strip best creates an ideal contour and encourages bonding without voids. For class V composite restorations resulting in recurrent caries or further demineralization and loss of restoration: • Lack of removal of the entire demineralized cervical aspect of the lesion • Placed composites rather than full coverage crowns in noncompliant patients with high caries risk • Not using retraction cord when indicated, resulting in a marginal void or crevicular fluid/hemorrhage contamination • Improper finish with ledge, flash, or roughness trapping plaque	

16.7 Composite Strip Crowns

Strip crowns commonly only provide temporary satisfaction with parents due to wear, discoloration, recurrent caries, and esthetic failures. The patient below had strip crowns placed under general anesthesia at age 2. Now at age 4, the parent is not satisfied with the esthetic presentation and was referred for zirconia crowns (Fig. 16.9).

Strip crown placement technique
1. Choose a strip crown size prior to beginning the prep and consider the entire presentation of the child's mouth (space loss from caries, crowding, overbite, and overjet).
2. Disking of the mesial surfaces of the primary canines may be necessary to provide the best esthetics and address incisor liability. Complete this prior to initiating incisor prepping.
3. Ensure the prep is complete, the pulp is treated as needed, and all enamel has been abraded with diamond flame bur to enhance retention.
4. Trim the crown as needed.
5. Create a small hole or holes with a small bur on the incisal edge of the strip crown for excess composite to escape.
6. Wash and dry the tooth prior to strip crown try-in and ensure the strip crown is clean and dry.
7. Manage hemostasis as needed (pressure, Superoxol, Astringedent™, etc.).
8. Etch for 30 seconds with 37% phosphoric acid.
9. Bond.
10. Place hybrid/packable composite in the strip crown.
11. Place the strip crown on the tooth, pressing firmly to engage all surface areas of the tooth.
12. Wipe the excess composite from the incisal edge and gingival margin (gently trying to avoid gingival hemorrhage) with a composite instrument (PF1 has ideal angling).
13. Polymerize with meter-tested curing light or lights from facial and lingual to reduce polymerization shrinkage (decreases potential sensitivity) if it is a large restoration.
14. The provider should be mindful of dental auxiliary polymerizing technique as their view and access is not as ideal as the doctor's and often the light is angled, causing inconsistent intensity in contrast to that of being perpendicular to the material.
15. Use a scaler or caries excavation spoon to remove the strip crown.
16. Finish the cervical area with a finishing flame to ensure no overhangs and finish the incisal edge where the composite was expressed during seating.
17. Perforated metal strips are best to finish interproximal areas and ideal for the contour of line angles. Metal finishing strips may also be used to re-introduce embrasures if they were lost with the strip crown anatomy.

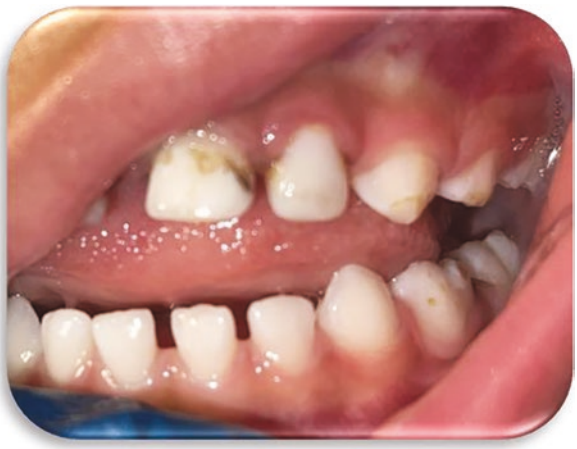

Fig. 16.9 Strip crown on a maxillary left central incisor after 2 years

16.8 Glass Ionomer Restorations

Glass ionomers have the same indications as composites, except they do not require etching when used alone. It is important to understand that a child whose dental disease has progressed to the point of requiring pulp therapy may not be the most compliant of patients regarding follow-up. Some practitioners enjoy placing glass ionomers as a temporary restorative measure (Interim Therapeutic Restorations-ITR). However, it takes negligibly more time to complete a definitive restoration and it is recommended, particularly in situations of pulp therapy to ensure the continued seal and success of the pulp therapy, esthetics, and continued asymptomatic status of the child.

16.9 Sandwich Restorations (Glass Ionomer and Composite)

Glass ionomer with composite resin (the sandwich technique) is a good choice for partially erupted teeth, subgingival caries in children who cannot get stainless-steel crowns (due to special healthcare needs and the necessary use of an MRI), or children who are not candidates for zirconia crowns (Fig. 16.10). Place a small increment of glass ionomer first if it is impossible to prevent crevicular fluid or blood contamination at the gingival cavosurface margin due to partial eruption, gingivitis, or subgingival caries. Then, complete the restoration with composite. Consider placement of an orthodontic band for extracoronal support and to ensure long-term restoration success.

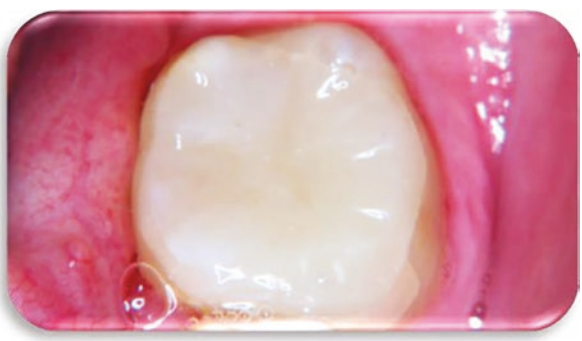

Fig. 16.10 Sandwich restoration (glass ionomer and composite)

16.10 Stainless-Steel Crowns (SSCs)

Stainless-steel crowns have served the needs of children's oral health for many years with positive predictable outcomes and minimal patient cooperation and clinician experience and skill needed. The only contraindications include nickel allergy, the artifact it would create in a possible future MRI, and parents preferring the highest level of esthetics (wanting only tooth-colored restorative materials) [11].

Below is a child referred to a pediatric dentist after recurrent caries and loss of a composite resin restoration. Illustrations below delineate the steps to the combination of MTA pulpotomy and stainless-steel crown placement (Fig. 16.11a–k).

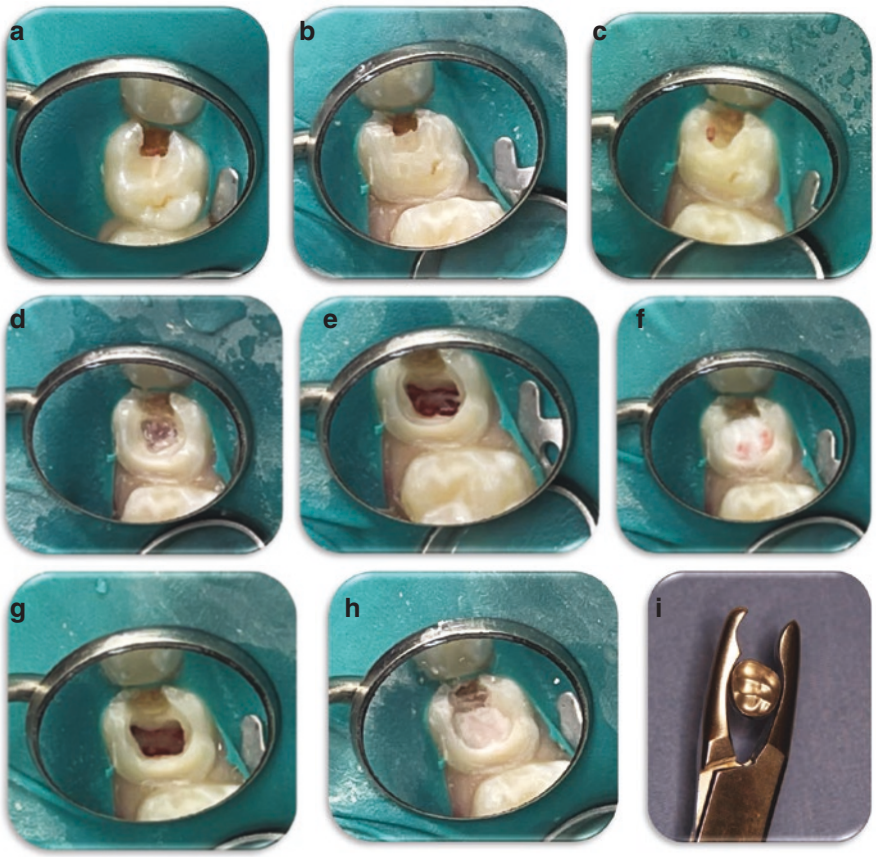

Fig. 16.11 (**a**) Failed class II composite resulting in carious maxillary second primary molar requiring vital pulp therapy and a stainless-steel crown. (**b**) Occlusal reduction opening access for caries removal. (**c**) Pulp exposure after complete caries excavation. (**d**) Pulp chamber is unroofed. (**e**) Pulpotomy performed using a round bur with a slow speed handpiece. (**f**) Sterile cotton pellets for pressure hemostasis. (**g**) Complete heme control, ready for pulp medicament. (**h**) MTA is packed in the pulp chamber. (**i**) Example of contour plier to assist on crown fitting. (**j**) Example of crimping of crown margins to enhance retention. (**k**) Stainless-steel crown cemented and cleaned

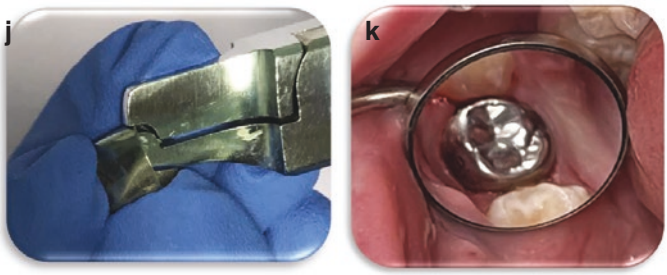

Fig. 16.11 (continued)

MTA pulpotomy and SSC placement

1. Choose a preliminary crown size prior to beginning the prep and consider the entire presentation of the child's mouth (space loss from caries, crowding, overbite, and overjet if restoring primary anterior teeth [including canines with stainless-steel crowns or pre-veneered stainless steel crowns])
2. Reduce the occlusal/incisal surface and open pits and fissures to ensure access to caries with a football diamond bur or other bur of choice.
3. Complete caries removal with a slow speed handpiece using a 4 round or larger bur being sure not to completely remove interproximal caries. This could create gingival hemorrhage prior to the pulp being addressed (note exposure of the mesial-buccal pulp horn in illustration).
4. Utilizing the football diamond (to eliminate a bur change) or a 330 carbide bur, unroof the chamber and assess the visual presentation of the pulp (note that Fig. 16.11d is an ideal presentation of a vital pulp).
5. Remove the pulp from the chamber with a 4–6 size round bur in a slow speed handpiece with copious irrigation utilizing sterile or treated water.
6. Pack sterile cotton pellets tightly for pressure hemostasis.
7. Upon removal of sterile pellets, pulp stumps should not be hyperemic and the pulp chamber should be clear of any pulp remnants or debris.
8. Pack MTA firmly against the floor of the pulp chamber with damp cotton pellets ensuring each pulp stump has the MTA sealed against it to promote dentinal bridging (a 2.0 mm thickness of MTA is recommended). After pulp treatment, place glass ionomer cement between pulp treatment and crown if there is concern of washout of the pulpal medicament.
9. Only after pulp management should a provider continue with caries removal near the interproximal gingival area or preparation of any portion of the crown that may create gingival hemorrhage.
10. Step through interproximal surfaces using a 69 L or flame diamond or lighten the contact with a football diamond in initial occlusal reduction and extension of grooves to expose the caries (as shown in Fig. 16.11b to eliminate a bur change).
11. Create a feather edge circumferentially around the tooth using a flame diamond noting that stainless-steel crowns generally require little, if any, buccal and lingual/palatal reduction.
12. Try on the crown.
13. Adjust the size as needed and utilize the hinge of a contour plier to reduce the crown width mesial-distally in situations of space loss (versus a Howe or 110 plier that does not create as ideal of a contour and may create divets that trap plaque) (Fig. 16.11i).
14. Utilize a crown crimping plier to tighten cervical collar to enhance crown fit.
15. Cement with a glass ionomer cement and ensure the crown is fully seated. In some situations, when used with caution, a band pusher can assist in full seating. Although more expensive, brands which provide an ampule automated mix option remove the mixing errors and increase efficiency. Prior to filling the clean crown, fill the remaining portion of the chamber and access with cement and then fill the crown, ensuring the cement is drawn up to the margins prior to placing.
16. Stainless-steel crowns adapted ideally will have a "snap" fit to create the best seal, reduced cement washout, and long-term retention. Pre-veneered stainless steel crowns must have a passive fit. Remove excess cement.

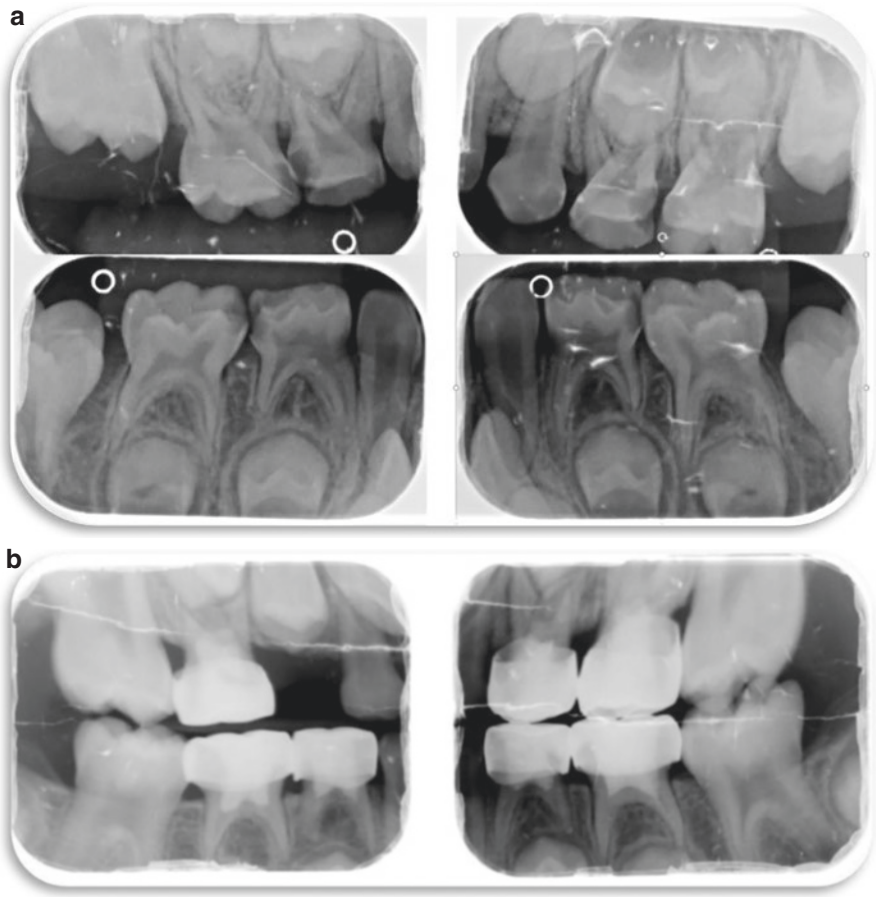

Fig. 16.12 (**a**) Preoperative images of a multiple primary molars with deep carious lesions requiring pulp therapy and crown coverage. (**b**) 2-year postoperative showing radiographic success of primary molars after MTA pulpotomies and stainless-steel crowns

The child below is an example of multiple teeth treated with MTA pulpotomies and bitewing radiographs preoperatively and again 2 years after treatment was completed. A band-and-loop was removed prior to bitewing X-rays at this 2-year recare appointment. Due to subgingival cervical caries, a size larger than planned was required on tooth J (65). Note the MTA engagement with each of the pulp stumps to create tiny "legs" radiographically (Fig. 16.12a, b).

Below is an example of full coronal coverage after MTA pulpotomy treatment due to trauma to the chin (Fig. 16.13a). Treatment is the same for a pulpotomy due to trauma as any pulpotomy and crown placement, with the exception of the fact that there is no caries removal and it is only addressing the pulp and prep. The child had an MTA pulpotomy versus a direct pulp cap or partial pulpotomy due to two weeks passing after the parasymphysis trauma, resulting in a complicated oblique fracture of tooth L (64) with pulpal exposure not diagnosed at the hospital (Fig. 16.13b). The post-op film is 2 years after the initial injury (Fig. 16.13c).

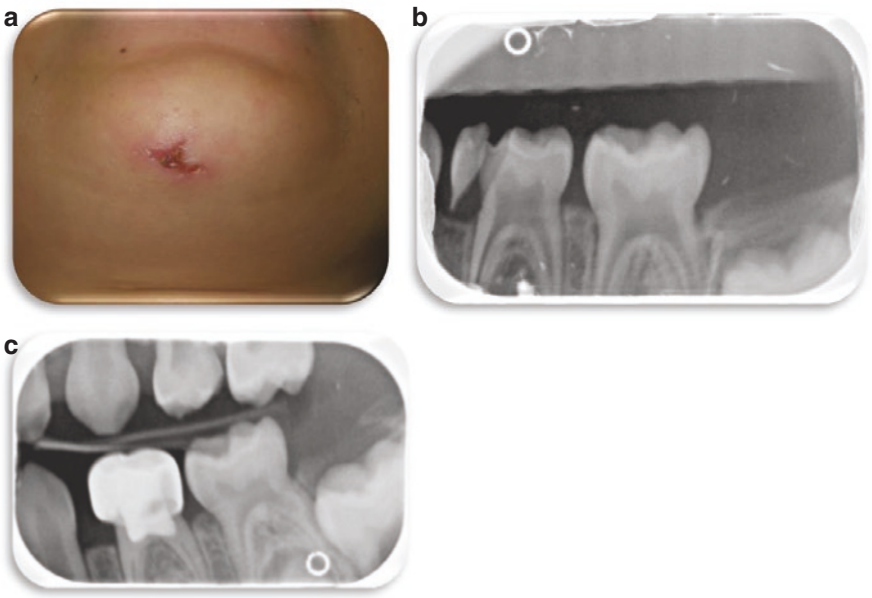

Fig. 16.13 (**a**) Trauma to the chin. (**b**) 2 weeks post-trauma showing complicated crown fracture on the mandibular left primary first molar. (**c**) 2 year post-op radiograph of the successful pulpotomy and stainless-steel crown coverage (note healing dentinal bridging)

16.11 Pre-veneered Stainless Steel Crowns

The technique is the same for pre-veneered SSCs as it is for traditional stainless-steel crown preps, except these crowns may not be squeezed to reduce mesial-distal crown width. Care must be taken to not crimp near the junction of the resin facing, and these crowns should be placed with a passive, not snap fit, to ensure resin facing is not flexed or compromised. These crowns may not be used with anterior crossbite in occlusion or in children who have a habit of chewing on non-food objects. They are an exceptional choice for maximum retention with minimal tooth structure remaining due to the ability to crimp the lingual collar. Although lower incisor pre-veneered crowns are not manufactured, it is possible to use uppers on lowers if size, space, and overjet (or removal of maxillary anterior teeth) allows. The child below had a submucosal cleft requiring oral intubation. After silver diamine treatment arrested caries, only a pulpotomy was required to reach healthy pulp tissue in the child, who was not a candidate for a pulpectomy due to incomplete root formation (Fig. 16.14a–c).

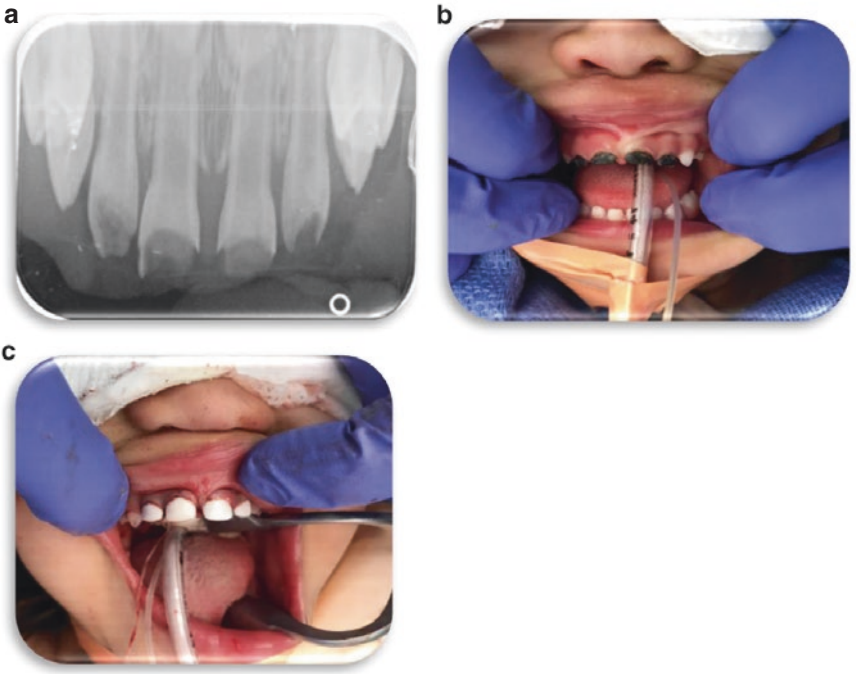

Fig. 16.14 (**a**) Pre-op radiograph showing severe early childhood caries affecting maxillary primary incisors. (**b**, **c**) Intraoperative view before and after pulpotomy and complete pre-veneered stainless steel crown coverage

16.12 Zirconia Crowns

Currently, zirconia crowns are the most durable and predictably-esthetic restoration available for anterior and posterior teeth. The high strength resin polymer crowns are esthetic and easier to place than zirconia; however, due to flexing properties, these crowns will likely never achieve as superior of esthetic properties as zirconia. Zirconia crowns may be used in any situation a SSC is indicated, pending the clinician's experience and comfort level. Zirconia crowns are especially useful in single, double, and triple anterior crown needs whereas pre-veneered are not as esthetic unless all four incisors are crowned. Zirconia crowns will not wear in a crossbite as pre-veneered crowns will. The 2-year-old patient below had the first photo taken immediately post-op (Fig. 16.15a) and the second photo 2 years later (Fig. 16.15b).

Due to the reverse nature in fitting in comparison to a stainless-steel crown where the crown may be adapted to a tooth and its prep, a zirconia crown prep must be adapted to the internal surface of the crown. This detail is what leads to the learning curve for providers that is steeper than other crown preps. Clinicians may require conscious sedation or general anesthesia to place zirconia crowns initially, particularly in cases with space loss, back-to-back crowns, and/or full mouth cases.

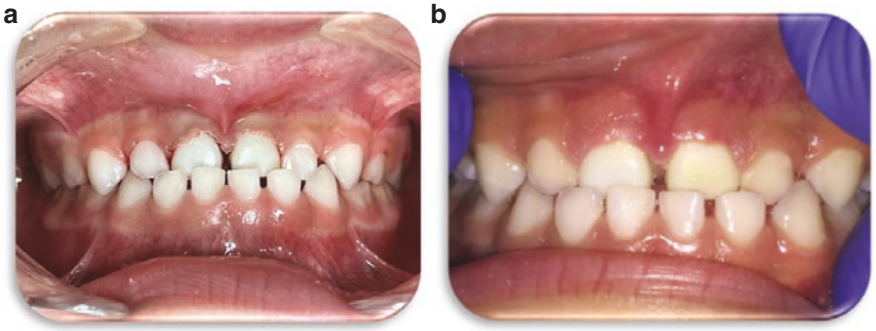

Fig. 16.15 (**a**) Immediate post-op image of maxillary central incisors restored with zirconia crowns. (**b**) 2-year post-op showing the crowns' continued success, despite crossbite and inadequate oral hygiene

Zirconia crown placement
1. Choose a preliminary crown size based on the mesial-distal dimension (utilize the "try-on" crown if the brand has one to keep the definitive crown clean of debris and enhance the bond).
2. Reduce the occlusal/incisal surface by 2.0 mm and open pits and fissures to ensure access to caries with a football diamond bur.
3. Caries removal/with a slow speed handpiece and pulp treatment (glass ionomer cement between pulp treatment if a eugenol-based pulp material is used or there is concern of washout of MTA).
4. Manufacturers recommend depth cuts with a chamfer bur to ensure adequate reduction and then connection of depth cuts to create a chamfer margin circumferentially.
5. Using a flame diamond bur, transition the chamfer margin to a feather edge margin.
6. Final fit of try-on and prep adaptation (err on infra-occlusion versus supra-occlusion due to the inability to create a snap fit).
7. Cement (follow manufacturer's cementation instructions) after remembering to fill the pulp chamber and access and ensuring the cement is drawn up to the margins of the crown prior to placing with a dual cure glass ionomer or hybrid cement and after 10–15 seconds of dentinal tubule engagement spot cure.
8. Remove excess cement and floss before final cure.
9. Final cure and thorough cleaning.
10. If the opposing dentition is primary natural dentition, utilize a bur to make minor occlusal adjustments on the opposing primary dentition or allow for natural occlusal equilibration.
11. Do not adjust zirconia crowns as this will create a spark and fire hazard as well as remove the gloss that is responsible for enhanced esthetics and promotes easy removal of plaque.

Discoloration from MTA (if not non-staining brand) and silver diamine fluoride will show through zirconia and must be completely removed prior to cementation if the parent expectation is uniform color (Fig. 16.16a, b).

Unlike stainless-steel crowns, zirconia requires much more prepping. However, this does not mean all teeth restored with zirconia require pulp treatment. Pulp treatment is only indicated if needed for reasons outside of crown prepping. Parents

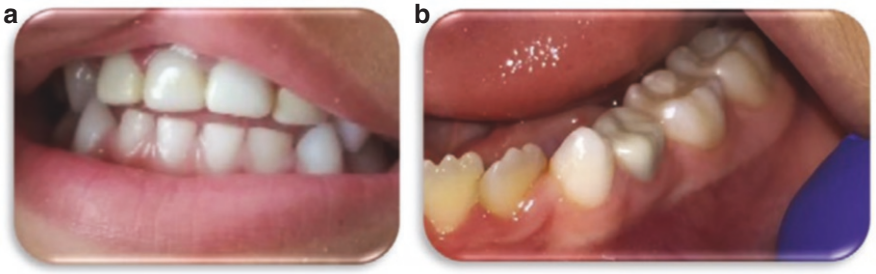

Fig. 16.16 (**a**) Right maxillary central incisor showing a zirconia crown placed over treatment with silver diamine fluoride. (**b**) Discolored zirconia crown on the mandibular left primary molar as result of MTA (not non-staining brand) staining

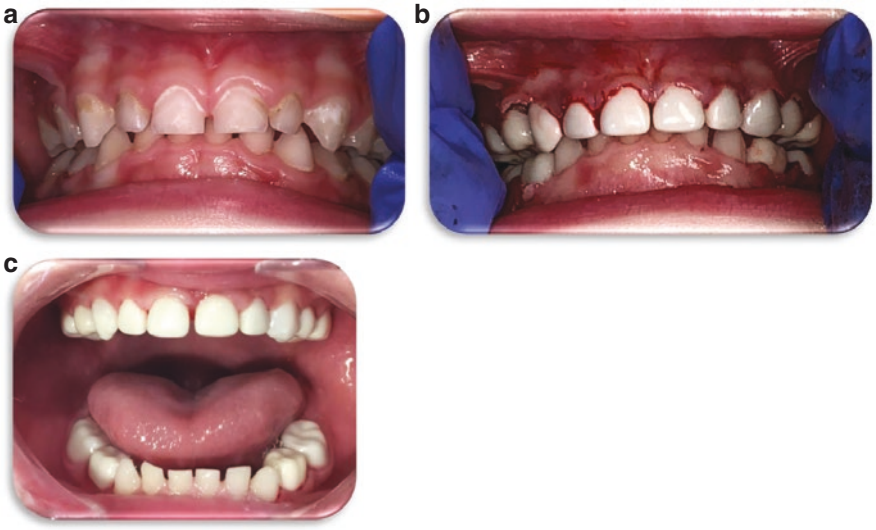

Fig. 16.17 (**a**) Preoperative view of early childhood caries. (**b**) Immediate post-op after zirconia crown restorations placed on maxillary incisors, maxillary canines, maxillary and mandibular primary molars. (**c**) One-week post-op view

must understand, particularly in situations such as the child below with extensive cervical caries requiring pulp treatment (Fig. 16.17a), that the tissue will look traumatized immediately postoperatively (Fig. 16.17b). As zirconia is more tissue-friendly than any other crown material, it will heal rapidly (Fig. 16.17c). Below is a patient preoperative, immediately postoperative, and at a 1-week surgical follow-up.

16.13 Final Tips

In situations of severe early childhood caries, providers need to think comprehensively about the needs of the child, desires of the parents, materials available, their skills and comfort level in restorative options, and their skills and comfort level in care delivery modality (conventional to general anesthesia). When teeth are severely broken down and require extensive pulp therapy and restorative, it is key to begin in the posterior on one side (particularly under general anesthesia) to regain vertical dimension prior to moving to the anterior. This will prevent inadvertent maxillary incisor flare when restoring anterior teeth that may be in occlusion with lower anterior teeth prior to regaining the vertical dimension. Providers must also be mindful not to create functional interferences resulting in crossbite with crown placement of primary canines. Unlike the stainless-steel crown below, a zirconia crown will not wear (Fig. 16.18).

Occlusion is difficult to check under conscious sedation and general anesthesia. It is a good practice to err on infra-occlusion with primary canines during zirconia cases. Better yet, Dr. Ron Bell, a dual board-certified pediatric dentist and orthodontist, coined the term "Cuisinart Dentistry". This is the mesial and distal disking of caries or simple space borrowing from primary canines (assuming the pulp as well as facial and lingual surfaces were not involved) to better allow addressing first primary molars pulpally and restoratively to fully save the space for the first premolar in the future. This technique may also allow incisor crowns to be placed more esthetically. This technique also makes it possible to place zirconia crowns in situations of significant space loss from caries. Similarly, an over-prepping, or early use of E-space of the second primary molar with more predictable pulp morphology may lend to the ability to best pulpally and restoratively treat a first primary molar that at first glance may appear non-restorable.

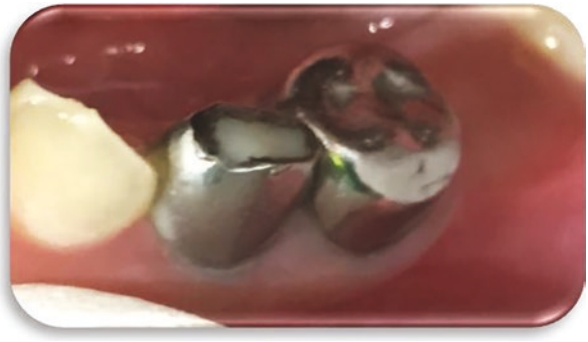

Fig. 16.18 Traumatic occlusion over stainless-steel crown creating wear of the crowns

Restorative options for primary teeth requiring endodontic treatment	
Fillings	Full coronal coverage
• Anterior and posterior teeth requiring indirect pulp caps for 1 or 2 surfaces in children who may be treated without conscious sedation or general anesthesia or <2 years to exfoliating the teeth • Posterior teeth treated with indirect pulp caps or pulpotomy for class I lesions with interproximal surfaces intact (recommended if >2 years to exfoliation to place an orthodontic band for long term extracoronal support)	• Any pulpectomy • Any pulpotomy • Any tooth in a young child treated with conscious sedation or general anesthesia • 2 or more surfaces with an indirect pulp cap • Any tooth requiring pulp treatment with >2 years to exfoliation • Any tooth that the child's cooperation does not predict positive clinical outcome for a filling • Any tooth with a failed filling due to recurrent caries, gastroesophogeal reflux disease, or habits • Any anterior tooth involving the incisal edge

16.14 Conclusion

Restoring mouths of children with significant dental disease requiring pulp therapy can be challenging. The great news is that it gets easier with experience, provided that the clinician continues lifelong learning utilizing evidence-based pulpal and restorative materials available to them. The clinician may need to embrace learning curves with materials that were not available to them in their training. Doing so will provide their patients with optimal contemporary esthetic restorative care.

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Endodontic Treatment for Young Permanent Teeth

17

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Contents

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A young permanent tooth is a recently erupted permanent tooth with incomplete root formation. These teeth may present different stages of root development ranging from a tooth with a wide root canal, open apex and thin walls, to a fully developed root with a slightly open apex [1].

Injury to the dental pulp of immature teeth is usually a result of dental trauma or a carious lesion.

The main objective of treatment in young permanent teeth is to preserve the tooth involved in the dental arch to allow proper maxillofacial development.

The endodontic treatment of young teeth is complex and challenging because of the unique characteristics of these teeth.

17.1 Factors Affecting the Treatment of Young Permanent Teeth

17.1.1 Pulp Characteristics of Immature Permanent Teeth

The dental pulp is a connective tissue of mesenchymal origin encased in a rigid chamber consisting of enamel and dentin [2]. In young teeth, the pulp space is wide and contains loose connective tissue rich in blood vessels and cells. This pulp tissue has high healing potential as it manifests superior cell proliferation and differentiation and the formation of blood and lymphatic vessels. The defense mechanism in the young pulp is more developed and potent. These characteristics are regulated by various extracellular matrix (ECM) bioactive molecules and growth factors [3].

17.1.2 Nature of Pulp Damage

Pulp injury can result from damage to the blood supply (dental trauma, excessive orthodontic forces, etc.) or damage to the protective enamel and dentin layer (e.g., crown fracture, caries, developmental malformation, MIH) [4]. Pulp reaction to

injury due to caries is different from traumatic injury. Changes in the pulp after exposure to caries result from the ingress of bacteria and their endotoxins. The inflammation of the pulp is accompanied by tertiary dentin formation [5]. However, after a traumatic dental injury, the depth of inflammation is limited to the superficial area of the pulp. Cvek demonstrated in 1982 that after pulp exposure due to complicated crown fracture, the depth of inflammatory cell infiltration after 7 days was only up to 2.2 mm with a hyperplastic defensive tissue reaction [6, 7].

17.1.3 Stage of Root Development

The stage of root development is a significant factor in the pulp's ability to heal and the determination of the appropriate treatment. Nolla classified the degree of tooth maturation in 1960; this classification is based on the radiographic evaluation and includes ten stages. Stages 7 refers to only one-third of the root completed, whereas stage 10 describes the fully developed root [8]. Understanding the stage of root development may aid in treatment decisions. The more immature the root, the younger the pulp; therefore, its healing potential is more prominent (see above). Furthermore, the blood supply to the pulp tissue flows through the apical foramen with no collateral blood vessels [2]. In a mature tooth, when the blood supply is damaged, pulp necrosis is expected, while in a young tooth with an open apex, recovery and even revascularization after pulp necrosis is possible, thus maintaining pulp vitality [9, 10].

The immature tooth may be characterized by thin dentinal walls and an unfavorable crown-root ratio [11, 12]. These teeth are more prone to trauma, especially in the cervical area. Cervical fracture is possible even as a result of masticatory forces [11]. Therefore, in younger, less mature teeth (Nolla stage 7 or 8), (Fig. 17.1b), it is imperative that the treatment plan will aim to enable maturogenesis. Furthermore, the susceptibility of the immature tooth to infection is increased due to the thin dentinal walls and the wide tubuli resulting in inflammatory root resorption after pulp necrosis [13].

17.1.4 Restorability

The treatment plan is directed by the extent of coronal damage and the ability to restore the tooth. Traditionally, the restoration of widely damaged teeth required the placement of a core and post, thus necessitating a root canal treatment. It is now well accepted that a 2 mm ferrule is more important than the post and core, thus enabling a more conservative approach to the teeth restoration [14].

An orthodontic evaluation is required, especially in teeth with poor restorative prognosis. Factors such as teeth crowding in the developing dentition may influence the decision to treat or extract the injured tooth. Moreover, early extraction of the damaged tooth may enable the eruption of the adjacent tooth into the extraction site,

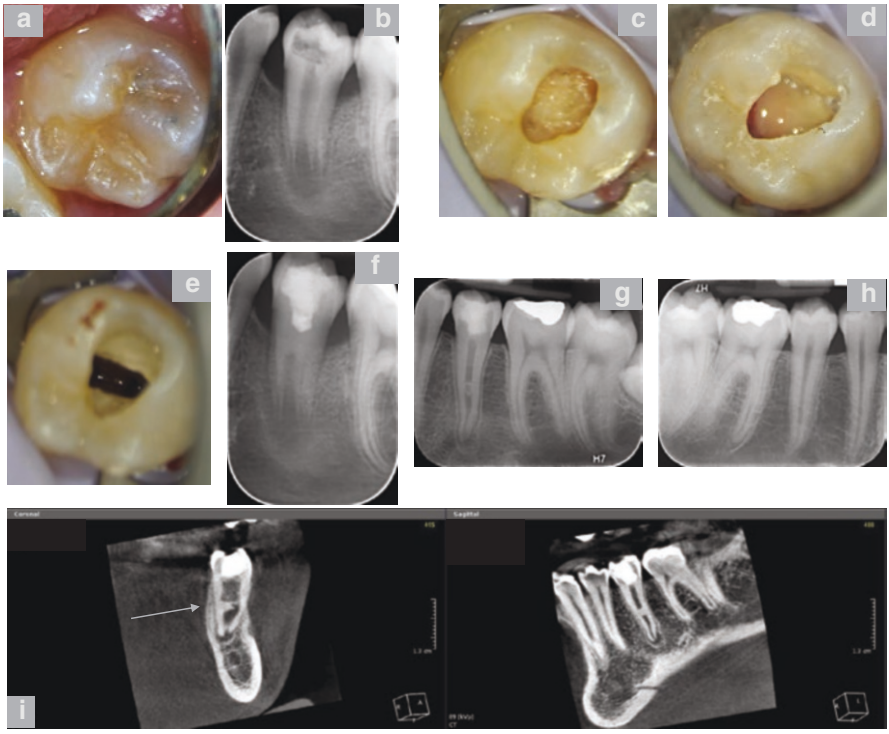

Fig. 17.1 Deep pulpotomy with $Ca(OH)_2$. (Courtesy: Dr. Eyal Nuni). (**a**) An 11-year-old boy complaining of spontaneous severe pain (irreversible pulpitis) has been taking analgesics for the last 4 days. Occlusal view of the second lower left premolar. A gray discoloration can be seen mesial to the transverse ridge. (**b**) Preoperative radiograph presenting pre-eruptive intra-coronal resorption, an immature root with very wide apical foramen (Nolla stage 7). (**c**) The resorptive lesion after access cavity preparation. (**d**) Pus drainage after pulp exposure. (**e**) Pulp tissue hemostasis after deep amputation. (**f**) Post-op radiograph calcium hydroxide placed on the pulp tissue and covered with Fuji IX™ glass ionomer. (Use of $Ca(OH)_2$ was decided to enable re-entry, considering the depth of pulp amputation). (**g**) 4.5 years' follow-up. Root development is almost complete. Hard tissue barrier in the middle of the root. The calcium hydroxide has been completely dissolved. A small apical radiolucency is present. (**h**) The contralateral radiograph demonstrates complete root development of the contralateral tooth. (**i**) CBCT demonstrating the incomplete hard tissue barrier (arrow) and the anatomy of the open apex

especially when maxillary molar teeth are involved. Extraction of hypo-mineralized teeth affected by MIH and spontaneous eruption of the second molar is an excellent treatment alternative, mainly if performed before the eruption of the tooth [15].

17.2 Pulpal and Apical Diagnosis

Diagnosis of the pulp status is critical in determining the appropriate treatment of young permanent teeth. However, it is also the most difficult to establish. There are discrepancies between the pulp clinical diagnosis based on clinical signs and

symptoms, radiographic examination, and the histologic findings [10]. Furthermore, children's reaction to diagnostic tests such as cold, palpation, and percussion can be excessive and does not reflect the actual sensation [16, 17].

Upon arrival at the dental clinic, the patient or legal guardian should complete and sign a full medical and dental history form. The clinician will review the form with the patient and enquire about the chief complaint, the events that led to it, and to the visit.

17.2.1 Clinical Examination

The clinical examination includes extra- and intra-oral examinations and tests. When clinical examinations are performed, contralateral and adjacent teeth should be tested first as a control. Extra-oral swelling along with sensitive and enlarged lymph nodes on palpation may indicate the presence of extra-radicular infection as a result of pulp necrosis. Intraoral swelling can also point to pulp necrosis and more localized infection. Any swelling should be palpated to determine whether it is firm or fluctuant and whether it is localized or diffused. Chronic endodontic infection can drain through an intra- or extra-oral sinus tract. The sinus tract must be traced (usually using a gutta-percha point #30) in order to determine the origin of the infection [18, 19] or by inserting an orthodontic wire through an extra-oral sinus tract.

A percussion test may help to isolate the source of the pain as it indicates an inflammation of the periodontal ligament, mediated by nociceptive mechanism [20]. This may be a result of periapical disease or food impaction; however, percussion sensitivity does not accurately reveal the pulpal status. Teeth can become tender for reasons other than an endodontic disease, such as maxillary sinusitis, hyperfunction, dentoalveolar pain disorder, or orthodontic movement [21].

Periodontal and mobility tests are significant although they also do not indicate pulp vitality. Deep isolated periodontal probing is an indication of bone loss that can be a result of pus drainage from the periapical area of a non-vital tooth. Increased mobility can be a result of numerous reasons including periodontal disease, parafunctional habit, orthodontic forces, physical trauma, and infection of the periodontal ligament as a result of pulp necrosis [18].

17.2.2 Pulp Sensibility Tests

Pulp sensibility tests are an important factor influencing diagnosis and treatment. These tests are more challenging in children as their ability to comprehend and express the sensation is limited. Thermal tests (cold or hot), electric pulp testing (EPT), and direct dentin stimulation (cavity/drill test) are the most prevalent methods. These tests do not indicate the vitality (blood circulation) of the tissue and rather indicate neural response of the tissue. Some studies suggest that these tests cannot be used to identify the degree of inflammation in the pulp but rather assess whether the pulp is vital or necrotic. False-positive and false-negative results can

also occur, for example, after dental trauma or as a result of inadequate isolation. These tests can be helpful in locating the diseased tooth by replicating its symptoms [22]. It is recommended that additional findings such as crown discoloration and radiographic evidence of a periapical lesion should support the lack of sensibility when determining pulp necrosis in dental trauma cases [23]. All sensibility tests require isolation of the examined tooth to receive a reliable response. In thermal and EPT, before testing the suspected diseased tooth, the contralateral tooth and then a tooth that is considered normal adjacent to the suspected diseased tooth should be assessed. If possible, the test should be repeated after a 1-min recovery for a more objective result [22].

17.2.2.1 Thermal Tests

Normal response to thermal test (cold or hot) is a sensation that disappears immediately after the removal of the stimulus. Prolonged pain, no sensation, acute pain, and immediate severe pain are considered abnormal [18].

Cold Test

Cold test is the most frequent thermal test used today as it is easy to perform, readily available, reproducible, and reliable. Cold spray is mostly used as a means to provoke the stimulus although CO_2 snow stick is a very reliable tool as well; however, its manipulation is less convenient [24]. Cold application stimulates the fast-conducting Aδ nerve fibers, thus producing a sharp localized pain. The test does not injure the pulp or cause damage (e.g., cracks) to the hard tissues [22]. The cold spray is applied to the tooth with a #2 cotton pellet touching the buccal surface [18, 25]. It should be taken into consideration that a multirooted tooth can respond to cold testing although the pulp tissue in some of the canals can be necrotic [26].

Heat Test

Heat application stimulates the slow conducting C nerve fibers located deep in the pulp, thus producing dull lingering pain. Although having a greater potential for pulp damage, the application of the heat source correctly will not injure the tissue. Heat can be applied by placing a warm gutta-percha stick on the buccal aspect of the isolated tooth or by applying hot water via a syringe after placing a rubber dam. Heat tests are most effective when the patient's main complaint is pain from hot stimuli. In these cases, the test will enable locating the tooth by reproducing the pain sensation [18, 22].

17.2.2.2 Electric Pulp Test (EPT)

EPT stimulates the Aδ nerve fibers by producing sufficient electric current to overcome enamel-dentin resistance [27]. In order to obtain a reliable test result, strict isolation (e.g., rubber dam) is needed. Without isolation stimulation of the adjacent teeth or periodontal ligament with the electric current can induce a false-positive response. None of the studies available indicated whether the readings on the device numerical display are reproducible and have any significance [22].

Nevertheless, a recently published paper evaluated the response of 1200 young permanent incisors in patients aged 6–12 to EPT. The EPT reading decreases with the development of the tooth. Regardless of the stage of root development, the lowest EPT thresholds were obtained when the EPT probe was placed on the incisal third of the crown [28]. This was attributed to the fewer number of mineralized axons in the immature pulp. Until innervation is completed (4–5 years of tooth in function), the electric pulp test is not a reliable means for determining tooth vitality [29].

Whereas all 1200 incisor teeth in patients aged 6–12 responded positively to EPT, the electric pulp testing was less reliable than Endo Ice and CO_2 snow in young patients (9–13) with immature premolars [28, 29]. Furthermore, Bastos et al. demonstrated that in traumatized young teeth (patients mean age 10.6 ± 3.3) the EPT was more reliable than cold testing with Endo Frost (Roeko, Langenau, Germany) or heat testing with gutta-percha. The authors reported a temporary loss of sensibility, especially after luxation injuries. The time until a positive response to sensibility testing was obtained ranged between 2 and 67 months [30].

When a negative response is obtained, EPT is most accurate in predicting pulp necrosis in any current intensity [31]. Weislede et al. (2009) demonstrated that when the EPT was used in combination with Endo Ice and CO_2 snow, the results were more accurate compared to the use of each of the tests separately [32]. Using EPT and cold test together will corroborate the result of each individual test. A negative response to both tests in a mature tooth will most likely indicate that the tooth is necrotic [33, 34].

17.2.2.3 Laser Doppler Flowmetry (LDF)

LDF is a method to assess the presence or absence of blood flow in the dental pulp tissue by projecting an infrared light beam through the crown. It has some significant advantages compared to other test modalities as it is accurate, reliable, objective, reproducible, and not painful or does not induce damage to the pulp tissue [35–38].

LDF was found to be a highly reliable method in order to determine the pulpal health status. The stage of root development did not affect the reliability of the test. Alghaithy et al. advocated the use of LDP for clinical situations in which pulp sensibility tests are expected to be unreliable, particularly following traumatic dental injuries [24]. The limitation to the use of the LDF is its availability in dental offices and the fact that it is still cumbersome and requires a complicated procedure.

17.2.2.4 Test Cavity (Drill Test)

Test cavity is used only as a last resort in cases where the test results are inconclusive or when other sensibility tests are impossible to use. This test is invasive and irreversible. A small class 1 cavity preparation in posterior teeth or a palatal cavity in anterior teeth is drilled with a high-speed bur and copious water spray without anesthesia. If the patient reports pain when the preparation reaches dentin, the tooth is presumed vital, and the cavity preparation is restored. If no pain is provoked, the

tooth is necrotic and root canal treatment is indicated. This test reflects the presence of functioning nerve fibers and not blood circulation in the pulp and is also very subjective; therefore, care should be taken while performing the test and interpreting its results [39]. Occasionally, the test cavity reaches the pulp, which appears to be normal. In these cases, a direct pulp capping should be indicated. This procedure should be questioned in apprehensive young patients and may affect any future cooperation; thus, it should be performed only in rare cases [39].

17.2.3 Radiographic Examination

Radiographic examination can include several types of X-rays and in some cases more advanced imaging modalities such as cone-beam computed tomography (CBCT). It is an integral part of the diagnostic process and should be considered in conjunction with the rest of the information gathered to achieve correct diagnosis and prognosis. The appropriate diagnostic image should be achieved using adequate exposure parameters to estimate anatomy and pathologic processes or conditions such as peri-radicular disease. Diagnostic radiographs should be taken only after reviewing the patient's health and dental history and a thorough clinical examination [40].

The patient, especially young children, should be exposed to the minimal radiation necessary [40]. However, for detecting endodontic pathosis, two diagnostic radiographs are often required. Usually bitewing and periapical radiographs (e.g., for detecting caries depth, furcation involvement, and periapical status), two radiographs from different angulations (e.g., detecting the roots morphology), or radiograph of the contralateral tooth (e.g., to assess stage of root development) of the suspected tooth [18] (Fig. 17.1h).

The International Association of Dental Traumatology (IADT) recommends taking up to four radiographs in every trauma case [41]. In some trauma cases such as root fracture, an occlusal radiograph is indicated for better diagnosis.

Digital radiographs are recommended as they have important advantages such as low radiation, easy to obtain, no chemical processing, instant viewing, manipulation possibilities, and easy to send [18].

It was previously thought a radiolucent PA lesion which is a result of pulp necrosis can be detected in a radiograph only when bone lose extends to the junction of the cortical and cancellous bone [42]; however, it was later demonstrated that periapical lesions can be diagnosed from periapical radiographs before they have eroded the cortices while they are still limited to the cancellous bone [43].

Pulp pathosis may be present even when it cannot be demonstrated in the PA radiograph and can only be detected in CBCT images [44]. Furthermore, radiographic interpretation is highly subjective and varies depending on the clinician [45, 46].

In young permanent teeth, some conditions can mimic the appearance of pathologic apical radiolucency as a result of pulp necrosis (Fig. 17.1). Teeth with incomplete root formation demonstrate apical radiolucency representing the normal apical

papilla. Therefore, in case there is doubt as to the periapical diagnosis, comparison should be done with the image of the contralateral tooth. Also, in trauma cases transient apical breakdown (TAB) can be present manifesting periapical radiolucency and sometimes negative response to cold test and crown discoloration; these characteristics are reversible [47].

Panoramic radiographs can be advised in various conditions. For example, when a large finding is present, to see its full dimensions or when an overall evaluation of the oral cavity is needed. It is also suggested when the first permanent molar has a questionable prognosis and its replacement by the second molar is considered, the presence of a normal tooth bud can be demonstrated in the panoramic view. In cases when intra-oral radiographs are impossible to take, as a result of a gag reflex or poor patient cooperation, panoramic or extra-oral radiographs can be helpful [48].

17.2.3.1 CBCT

CBCT has become an important and common tool in dentistry and endodontic practice since it was first introduced at the beginning of the twenty-first century [49].

It enables three-dimensional imaging allowing the dentist to observe the tissues in multiple planes. When indicated CBCT should be used as an adjunct diagnostic tool in addition to intraoral radiography and not as a replacement. It is a valuable instrument in assessing periapical pathosis, dental trauma, anomalies in the developing dentition, oral pathology, etc. [40] (Fig. 17.1i).

Clinical guidelines for the use of dental radiographs and CBCT in children and adolescents [40] and in endodontics [50] were published. As in all imaging modalities, the ALARA (As Low As Reasonably Achievable) principle should be implemented when considering the use of CBCT, especially in children who are more prone to radiation damages [51].

Every case should be assessed individually in regard to selection of the use of CBCT. The benefits of the 3-D imaging should outweigh the potential risks and may be considered when conventional radiographs are inadequate to complete diagnosis and treatment planning [50, 52].

17.2.4 Pulpal and Apical Tissue Diagnostic Terminology

Endodontic diagnosis of the pulp and apical tissues is based on clinical and radiographic findings. This is elaborated in further detail in the glossary of endodontic terms published by the AAE [53]. The pulpal status was traditionally defined as either normal, reversible, or irreversible, referring to the ability of the vital inflamed pulp to heal. Later a differentiation was made between symptomatic or asymptomatic irreversible pulpitis. The diagnosis is based on objective and subjective findings.

According to the AAE glossary of terms, whereas in asymptomatic irreversible pulpitis, the inflammation is caused by caries, caries excavation, or a traumatic injury, without any clinical symptoms. Symptomatic irreversible pulpitis is accompanied by lingering thermal pain, spontaneous pain, or referred pain. In both cases, the pulp is incapable of healing [53]. However, since pulpitis is a progressive

disease, this classification does not refer to the gradual progression of the disease in the pulp, nor to the ability to remove only the diseased tissue, thus enabling the remaining pulp to heal. Therefore, the current classification does not enable the practitioner to assess the treatment outcome.

Wolters et al. in 2017 introduced a new classification system. This classification includes four stages of pulpal disease: initial, mild, moderate, and severe [54]. Initial pulpitis is characterized by prolonged response to cold testing without any additional findings. In case of mild pulpitis, there is a prolonged reaction to thermal stimuli, which can last up to 20 s and a possible sensitivity to percussion. Histologically, the inflammation is limited to the coronal pulp. Moderate pulpitis is marked by a longer response to thermal testing which can last for minutes. It may be accompanied by sensitivity to percussion and a spontaneous dull pain. The pain can be managed by analgesic medications. Histologically, extensive local inflammation confined to the coronal pulp can be expected. In severe pulpitis, a severe spontaneous pain with a strong reaction to thermal stimuli is often accompanied by throbbing pain. The patients complain of trouble sleeping that can be aggravated when lying down. The tooth is sensitive to percussion. A more extensive inflammation which may extend into the root canals may be reflected histologically. The authors suggest that the type of treatment should be adjusted to the diagnosis. Mild pulpitis can be treated by indirect pulp treatment. Partial or cervical pulpotomy is suggested in cases of moderate pulpitis, whereas cervical pulpotomy can be considered in severe pulpitis. Nevertheless, when the bleeding cannot be controlled, pulpectomy is indicated [54]. This suggested diagnoses and treatments should serve as general guidelines by the prudent clinician when treating the inflamed pulp.

17.3 Materials Used in Vital Pulp Therapy

17.3.1 Sodium Hypochlorite (NaOCl)

Sodium hypochlorite is the most common irrigation solution used in endodontics. It is usually used for root canal irrigation because of its effective antimicrobial and tissue-dissolving properties. It is used in various concentrations usually between 0.5 and 5.25% [55].

Currently it is also considered the most effective material used in vital pulp therapy for rinsing during the treatment and for hemostasis of the pulp tissue [56]. It disinfects the dentin and pulp, promotes hemostasis, and dissolves blood clots. Irrigation with NaOCl removes infected dentin chips and tissue remnants [57]. The presence of a blood clot may lead to internal resorption and dystrophic calcifications, serve as a substrate for bacteria in leaking restoration, and damage dentin bridge formation, thus compromising the treatment outcome [58]. Rinsing with sodium hypochlorite does not damage the pulp tissue or impair the ability to recruit pulp cells, their differentiation, and hard tissue deposition [59]. The ability to

control the bleeding after rinsing with NaOCl for 10 min can distinguish between reversible and irreversible pulpitis, and continuous bleeding is considered a sign of irreversible inflammation [57].

17.3.2 Ethylenediaminetetraacetic Acid (EDTA)

EDTA, a polycarboxylic amino acid, is one of the irrigation solutions used in endodontic procedures. This chelating agent removes the inorganic component of the dentin and smear layer [60]. It is used in a 17% concentration. It has an antibacterial effect which is stronger than 0.5% sodium hypochlorite but weaker than 2.5% sodium hypochlorite [61]. EDTA exerts its strongest effect when used synergistically with sodium hypochlorite [62]. Studies have demonstrated that EDTA can solubilize dentine matrix components, shows morphogenetic activity, and can induce reparative dentinogenesis [63].

Irrigation protocol combining sodium hypochlorite and EDTA enables the release of growth factors, cytokines, and other bioactive molecules required for dentinogenesis [64].

17.3.3 Calcium Hydroxide [$Ca(OH)_2$]

Calcium hydroxide was considered the gold standard material for intracanal medication and vital pulp therapy. Nevertheless, more recent studies questioned its effectiveness in further eliminating bacteria as a root canal dressing material [65–67]. For both purposes, it is usually mixed with sterile water or saline and dissolves into Ca++ and OH− ions. Its main properties include high pH (12.5–12.8), low solubility, tissue dissolution, long-term wide range antimicrobial activity, and inactivation of endotoxin [65].

The main drawbacks of $Ca(OH)_2$ are associated with its physical properties. This non-setting material will go through degradation and dissolution over time, leading to infection when coronal leakage is present (Fig. 17.1g). Furthermore, exposure of dentin to $Ca(OH)_2$ especially for long periods reduces its flexural strength and lowers its fracture resistance [65]. $Ca(OH)_2$ capping during vital pulp therapy in young permanent teeth is also associated with calcifications of the pulp, which makes future root canal treatment when needed difficult or even impossible [68].

17.3.3.1 Hard Tissue Formation

Calcium hydroxide's high alkaline values have been shown to cause fibroblast and enzyme stimulation, pulp tissue defense mechanisms and repair activation, as well as hard tissue formation in cases of pulp capping and apexification. In direct contact with the pulp, a superficial layer of tissue necrosis (up to 2 mm) occurs. Underneath only signs of mild inflammation can be observed.

During dentinogenesis growth factors, cytokines and other bioactive molecules are sequestered in the dentin matrix [69]. These compounds are released as a result of caries by the bacterial acids [70] and as a result of different rinsing solutions such as sodium hypochlorite and EDTA (see above). Transforming growth factor beta (TGF-β) family is one of the main growth factors considered significant in signaling dentin regeneration. Application of $Ca(OH)_2$ on dentin leads to TGF-β1 release, thus inducing dentinogenesis [71].

Recent studies in human teeth have found that new odontoblasts or odontoblast-like cells can't be detected histologically after direct pulp capping with $Ca(OH)_2$ or MTA. Therefore, the nature of the new hard tissue is not clear as it can be dentin or a dystrophic intra-pulpal mineralization in response to inflammation [72, 73]. The hard tissue barrier induced by $Ca(OH)_2$ placed on the pulp is porous and contains tunnel defects [74] (Fig. 17.1).

As $Ca(OH)_2$ is dimensionally unstable and disintegrates slowly over time. These tunnels can be a pathway for bacterial microleakage leading to pulp damage, dystrophic calcification, and eventually necrosis [65].

Hard setting calcium hydroxide cements (e.g., Dycal; Life, Kerr Hawe, Bioggio, Switzerland) are not recommended for vital pulp therapy. They induce lower pH and significant weaker antibacterial effect because of the lower release of OH^- ions [75]. They disintegrate with time, do not support the final restoration, induce more pulp inflammation, and have less hard tissue regeneration [57].

It is also not advised to use light curing $Ca(OH)_2$ (e.g., Ultrablend Plus, Ultradent, South Jordan, UT; Calcimol LC, VOCO, Cuxhaven, Germany) or calcium-silicate containing materials (e.g., TheraCal LC, Bisco, Schaumburg, IL) for vital pulp therapy. These materials are cytotoxic and have a significant lower pH [76].

17.3.4 MTA- and Calcium Silicate-Based (CSB) Materials (Bioceramics)

MTA was presented in the 1990s as the first CSB revolutionary material in dentistry [77]. It is derived from Portland cement and was indicated initially as a root-end filling material and with time has been recommended for pulp capping, pulpotomy, apical barrier formation in immature teeth, and root perforations repair. It consists of a hydraulic calcium silicate powder that sets in the presence of moisture. When mixed with water, $Ca(OH)_2$ and calcium silicate are formed causing its high alkaline pH [78, 79].

MTA is a bioactive material that is commonly used for vital pulp therapy because of some of its favorable characteristics. Most of the initial studies and recently available data are based on ProRoot MTA (Tulsa/Dentsply, Tulsa, OK). The material is hard setting and non-soluble. It forms a superior bonding to dentin by the formation of hydroxyapatite crystals that create chemical bonding between the MTA and the dentin. As a result, the material is biocompatible and has an excellent seal. Thus, it provides an additional protective layer in cases of coronal leakage, unlike $Ca(OH)_2$ [79]. It possesses some antibacterial and antifungal properties due to its high alkalinity [78].

The material promotes proliferation, differentiation, and activation of hard tissue-forming cells, thus inducing dentin formation and hard tissue repair in several mechanisms, such as the release of growth factors, cytokines, and bioactive molecules (see $Ca(OH)_2$) from the dentin and fibroblasts [80, 81].

As demonstrated with $Ca(OH)_2$, in an in vivo study of direct pulp capping with MTA in human teeth, the mineralized tissue formed was mostly atubular and did not display the features of regular dentin. No odontoblasts or odontoblast-like cells could be detected histologically [73].

MTA has a few drawbacks, mainly a long setting time (2–4 h), difficult handling properties, tooth discoloration which was demonstrated by either gray or white MTA, and difficulty to remove after setting [82]. It was shown that the hard tissue formation after the use of MTA was superior and caused less pulpal irritation than $Ca(OH)_2$ [83]. Furthermore, the long-term success after vital pulp therapy using MTA was better than $Ca(OH)_2$ [84, 85].

17.3.4.1 Biodentine and EndoSequence Root Repair Material

In recent years, a considerable number of new materials based on calcium silicate (bioceramics) were introduced into the market. It should be emphasized that the term MTA or bioceramic material is generic, and whereas many papers regarding several materials such as ProRoot MTA, Biodentine™, or EndoSequence root repair material were published, there is only limited information regarding some of the other materials. Therefore, before using a new material, the prudent clinician should study the current knowledge regarding this material.

These new materials have a few significant advantages in comparison to MTA. One of the important ones is their better handling characteristics and faster setting time. Biodentine™ (Septodont, Saint-Maur-des-Fossés, France) is presented in a form of a capsule containing powder and liquid that is mixed in a triturator. Its setting time is 12 min [86]. It releases Ca ions forming $Ca(OH)_2$ [87] and TGF-β1 from pulp cells [88] inducing proliferation, migration, and differentiation of human dental pulp cells [89, 90].

In conclusion, although $Ca(OH)_2$ has many favorable properties, calcium silicate-based materials are preferred over $Ca(OH)_2$ for vital pulp therapy. The use of newer materials instead of ProRoot MTA may be advised considering their improved characteristics.

17.4 Pulpotomy

Pulpotomy was defined by Finn 1959 as "the *removal* of a *coronal part of pulp* tissue followed by placement of a dressing or medicament that will promote healing and preserve the vitality of the tooth." Despite many technical changes made since its introduction by Sweet in 1930, the basic principles of pulpotomy have not changed [91]. The rationale behind this procedure is the gradual propagation of bacterial invasion into the pulp tissue.

Cvek et al. described in 1978 the pulpal reaction following pulp exposure after cavity preparation or crown fracture and calcium hydroxide dressing in monkeys. The depth of inflammatory changes was limited to 2–3 mm [92].

In the early stages of pulp disease and until the pulp becomes completely necrotic, there is coexistence of healthy and damaged pulp tissue [93, 94]. The coronal portion of the pulp may become necrotic, while the more apical tissue can remain vital, and only moderately inflamed.

The traditional indications for pulpotomy include the treatment of a carious tooth or traumatically exposed pulp, to allow preservation of vitality and function of the remaining pulp [7, 53] (Fig. 17.2). The periapical area appears radiographically normal, and hemorrhage is controlled. This procedure was limited to teeth which required only small- or medium-sized restorations [95]. Contraindications include teeth with spontaneous pain, periapical radiolucency, excessive hemorrhage, purulent or serous exudates, or pulp calcifications [95]. Teeth with interradicular bone loss or evidence of internal resorption were also excluded.

Initially, only teeth with normal pulp (e.g., iatrogenic exposure) or reversible pulpitis were treated by pulpotomy. More recently pulpotomy was also indicated for immature and mature permanent teeth in young adults with symptomatic and asymptomatic irreversible pulpitis, as well as teeth with periapical radiolucency, when only part of the pulp was affected [96–99] (Fig. 17.1). Bone resorption occurs as early as 15 days after pulp exposure and infection, after which the lesion stabilizes [100]. Periapical inflammation precedes total pulp necrosis and is a result of cytokines and inflammatory mediators extending into the periapical tissue. The removal of the inflamed pulp during pulpotomy can enable repair of the periapical lesion [101] (Table 17.1).

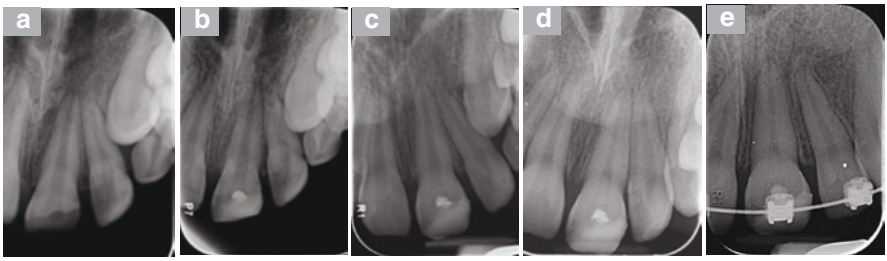

Fig. 17.2 Partial pulpotomy with a bioceramic material. (Courtesy: Dr. Iris Slutzky-Goldberg). (**a**) A 9-year-old girl was referred for treatment of the left central incisor immediately after a complicated crown fracture. A small pulp exposure was observed. The tooth was sensitive to percussion and highly sensitive to cold application. A periapical radiograph demonstrated an immature root corresponding to Nolla stage 9. (**b**) Partial pulpotomy with EndoSequence root repair material. A temporary flowable composite restoration was placed on top of the bioceramic material. (**c**) 3 months' follow-up demonstrates a calcified bridge 1 mm apical to the bioceramic material. The crown had been restored with a composite resin. (**d**) 6 months' follow-up—complete root maturation is evident with partial obliteration of the root canal space. (**e**) 3-year follow-up—the asymptomatic tooth during orthodontic treatment. Normal response to cold test was recorded

Table 17.1 Outcome of pulpotomy carried out with different materials

Authors	No. of teeth	Material and procedure	Etiology	Ages (mean)	Follow-up period (month)	Diagnosis	Success rate
Taha and Abdulkhader	20	Biodentine Full pulpotomy	Caries	9–17	6 months, 1 year	Irreversible pulpitis $N = 6$ + PA lesion $N = 14$	95%
Linsuwanont et al.	55	MTA	Caries	7–68 (29)	≤62 months	*All*	87.3%
						Immature teeth ($N = 10$)	100%
						Irreversible pulpitis	84%
						+ PA lesion	76%
Qudeimat et al.	23 Molars	MTA Full pulpotomy	Caries 20/23	7.6–13.6 (10.7)	18.9–73.6	78%	100%
						Irreversible pulpitis and apical periodontitis	53% bridge formation

Studies report the outcome of pulpotomy in various pulpal pathologies. The expected outcomes of the procedure are lack of signs and symptoms, combined with continued root maturation, dentin bridge formation, and healing of periapical rarefaction [97].

17.4.1 Clinical Procedure: Partial and Cervical Pulpotomy

This procedure should be performed only after more conservative treatment options, such as selective caries removal (previously described as indirect pulp capping, or direct pulp capping) were ruled out (see Chaps. 10 and 12).

The tooth should be anesthetized prior to the procedure. The type of anesthesia, either lidocaine and adrenaline or prilocaine without adrenaline, had no effect on the outcome [102]. The use of intra-pulpal anesthesia should be avoided in order to prevent damage to the pulp tissue [103]. In a meta-analysis published in 2018, local infiltration with articaine or lidocaine nerve block for pulpal anesthesia were found to have similar efficacy in pediatric dentistry, yet less postoperative pain was reported following articaine. No difference in the occurrence of adverse effects between the material was reported [104]. After rubber dam isolation, the tooth should be rinsed with sodium hypochlorite. The use of magnification and illumination, preferably with the dental operating microscope, is recommended. Following complete caries removal, or after traumatic crown fracture with pulp exposure, 2 mm of pulp tissue is removed using a new high-speed round diamond bur with water coolant (Fig. 17.2a). The use of a tungsten or carbide bur is contraindicated as not to tear the remaining pulp tissue [105]. The cavity and the pulp are rinsed with

sodium hypochlorite throughout the procedure. Visualization of the remaining pulp tissue must be done, as previously mentioned. This is followed by an attempt to stop the bleeding using a cotton pellet soaked in sodium hypochlorite for 5–10 min with light pressure. When hemostasis is achieved, a bioceramic material is placed over the amputated pulp [106, 107] (Fig. 17.3c, d). The use of a biomaterial that can cause crown discoloration should be avoided. Hence, materials such as Biodentine™ or BC EndoSequence root repair material should be preferred over MTA in esthetic regions. An immediate permanent restoration, such as glass ionomer or adhesive restoration, should be preferred [107, 108] (Fig. 17.3e).

Biodentine™, which is used as a capping material, can also fill the access cavity and serve as a temporary restoration. However, it is not indicated in cases of extensive coronal damage [108]. In a study of 41 patients, Biodentine™ was used during pulpotomy. In most of the cases, the setting time was longer than claimed by the manufacturer (12 min) and lasted on average 22 min, and in one of the cases as long as 45 min [109]. Furthermore, whereas bonding to 12 min matured Biodentine™ was shown to be weak and unsatisfactory, 72 h maturation or a delayed bonding of 2 weeks resulted in increased bond strength and a more clinically acceptable bond [108]. Placing the overlying definitive resin composite restoration is best delayed for at least 2 weeks to allow sufficient intrinsic maturation of the Biodentine™ to tolerate contraction forces from the resin composite [110].

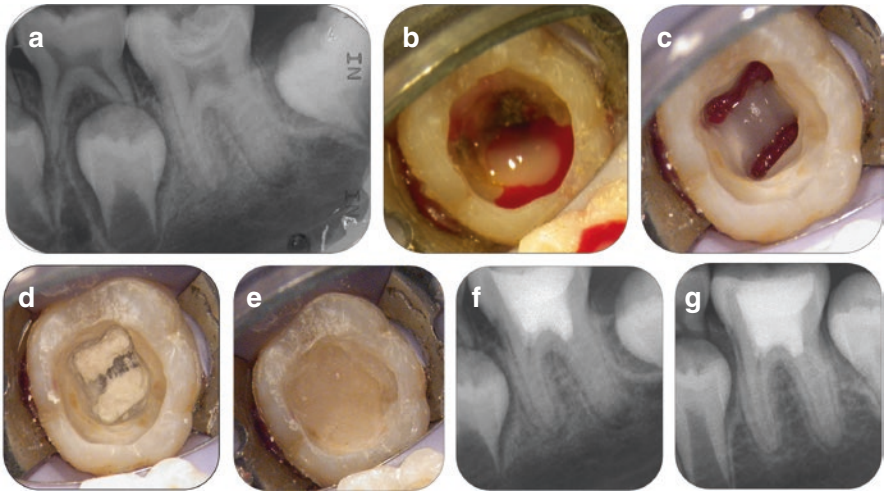

Fig. 17.3 Cervical pulpotomy with a bioceramic material. (Courtesy: Dr. Eyal Nuni). (**a**) A 7.5-year-old girl was referred for endodontic treatment of the first mandibular molar, due to secondary caries. The tooth was asymptomatic with a prolonged response to cold test. (**b**) Following caries removal and pulp exposure, bleeding and pus secretion were demonstrated. (**c**) Healthy looking pulp tissue was observed after cervical pulpotomy and sodium hypochlorite hemostasis. (**d**) Pulp capping with EndoSequence root repair material. (**e**) Fuji IX™ Glass ionomer was placed on top of the bioceramic material. (**f**) Post-op radiograph. (**g**) 13-month follow-up demonstrating complete root maturation

If the pulp continues to bleed, a stepwise approach is suggested: deeper amputation of the pulp tissue should be carried out, until normal-looking tissue is observed. The same procedure can be repeated, until reaching the canal orifices, thus performing a cervical pulpotomy (Fig. 17.3).

Nevertheless, in some cases, especially in traumatized teeth with wide canals, when the pulp in the canal orifices presents signs of inflammation, a deep pulpotomy below the root orifices may allow apexogenesis. Leaving vital tissue in the canal can encourage the continued physiological development and formation of the root end [53]. However the treatment outcome of this procedure is less predictable (Fig. 17.1). A meticulous case selection and the use of the operating microscope are obligatory [58].

17.4.2 Bleeding Time

One study compared the outcome of pulpotomies performed in 14–60-year-old patients using Biodentine™ in teeth diagnosed as either mild, moderate, or severe pulpitis according to Wolters classification [54] previously described. The authors found that the average time for hemostasis ranged from 1 to 4 min. Only a small difference in bleeding time was found between teeth with mild or moderate pulpitis. In teeth with severe pulpitis, an average of more than 2 min was required to stop the bleeding, although the difference between the groups was insignificant. The 1-year outcome was significantly better for the mild group compared with the severe pulpitis group [109].

17.4.3 The Expected Outcome

Successful pulpotomy, either partial or cervical, results in the maintenance of pulpal vitality. A hard tissue barrier is expected to be apical to the bioceramic material. The immature root continues to develop, and apexogenesis is usually observed (Fig. 17.2). The success rate of $Ca(OH)_2$ or MTA pulpotomy in immature teeth is between 90% [84] and 100% [111, 112], depending on the materials used and the follow-up period.

17.4.4 Pulpotomy with Different Materials

Different dressing materials such as $Ca(OH)_2$, MTA, and other bioactive materials, as well as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), are all used during pulpotomy. When MTA and $Ca(OH)_2$ pulpotomies were carried out within the same patient, the 12-month recall demonstrated 100% success for MTA as compared with 91% for $Ca(OH)_2$ [84]. A comparison of partial pulpotomy with MTA or Biodentine™ in 69 patients aged 6–18 with signs of irreversible pulpitis showed

similar success rates for both materials after a mean follow-up of 32 months (92% vs. 87% respectively, $p \geq 0.05$), although more discoloration was observed in the MTA group [113]. Similarly, the clinical and radiographic outcome of pulpotomy with white MTA or Biodentine™ in traumatized anterior immature teeth did not differ among the 7.5–9 years old patients. However, whereas no discoloration was observed in the Biodentine™ group at the 6-month follow-up, 23 of the 25 teeth that were treated with MTA developed coronal discoloration [114]. Comparable success rates for MTA pulpotomy were reported in another study as well [115]. A study that compared the effectiveness of three different pulpotomy agents: fast setting MTA (MM-MTA, Micro-Mega, Besançon Cedex, France), nano-hydroxyapatite (NHA) and platelet-rich fibrin (PRF) in immature permanent molars did not find a difference in the treatment outcome among the tested materials. At 12 months, all teeth demonstrated evidence of continued root maturation, although MM MTA and NHA had a higher tendency for canal obliteration [116]. Calcific metamorphosis was also reported following pulpotomy in teeth treated by either $Ca(OH)_2$ (2 out of 15 teeth) or MTA (4 out of 15 teeth), although not considered a sign of failure [84]. The radiographic outcome of pulpotomies in 60 permanent mandibular molars with signs of irreversible pulpitis that were treated with a light-cured calcium hydroxide (Dycal; ApaCal ART, Brussels, Belgium), EndoSequence root repair material, or PRF was evaluated after 6 months and a year. No statistically significant difference was observed in the outcomes of the three materials tested. Although clinically after 12 months, PRF and EndoSequence showed the highest reduction of pain mean score [117]. A meta-analysis published in 2019 compared different pulpotomy-dressing agents in the treatment of immature permanent teeth. After the screening of 1365 articles, five randomized clinical trials were included; comparable success rates were found between the calcium hydroxide, calcium-enriched material (CEM), PRF, and MTA, even though the authors reported a high risk of bias [118].

17.4.5 Timing of Pulpotomy After Traumatic Injuries

The classic paper published by Cvek et al. in 1982 suggested that pulp amputation can be carried out within a week after vital pulp exposure due to crown fracture [6]. More recently it was published that a delay of up to 9 days between the time of trauma and treatment is considered safe [7, 119]. Bimstein and Rothstein also concluded that an exposure size smaller than 4 mm does not affect the outcome of Cvek pulpotomy [7].

17.4.6 Prognostic Factors

A meta-analysis aimed to assess the prognostic factors affecting the outcome of partial pulpotomy in carious permanent molars found a success rate of 98% after 6 months, the success rate dropped after 2 years to 92%. The only significant prognostic factor was the preoperative pulp status. The authors stated that neither the

patient's age nor apical closure or the pulp capping material affected the treatment success rate. Indicating that partial pulpotomy can be a viable option for both mature and immature teeth [120].

Pulpotomy requires less chair time compared to root canal treatment and reduces the number of radiographs, therefore enabling better patient cooperation. In comparison, endodontic treatment, especially in immature teeth, may also require additional apexification. The simplicity of pulpotomy makes it less technique-sensitive thus more feasible and less costly than root canal treatment [121].

Restoration of the teeth is an integral part of vital pulp therapy. Long-term evaluation of the effect of the time span between vital pulp therapy and the final restoration shows that a shorter period predicts a better outcome [107].

17.5 Regenerative Endodontics

According to the AAE glossary of terms, these are "Biologically-based procedures designed to physiologically replace damaged tooth structures, including dentin and root structures, as well as cells of the pulp-dentin complex" [53]. In the endodontic literature, regenerative endodontics, revascularization, and revitalization are used interchangeably, although they describe different histologic outcomes [11].

In 2004 Banchs and Trope proposed a new protocol for revascularization of an abscessed mandibular premolar, using a triple antibiotic paste dressing. This included the induction of an intracanal blood clot and placement of an MTA plug on the blood clot [122]. This protocol was based on a previous study of Nygaard- Ostby in 1961, who induced bleeding into the root canal space [123]. The antibiotic composition used by Banchs and Trope was based on the finding of Hoshino et al. that studied the susceptibility of bacteria from infected dentin to different compositions of antibiotics [124]. Iwaya et al. in 2001 were the first group that applied the concept of revascularization to treat an infected immature permanent tooth with a chronic apical abscess. They treated the tooth by repeated dressing of the root canal space with ciprofloxacin and metronidazole. Thirty months after the initiation of the treatment, they demonstrated complete root formation [125].

The currently used protocol is carried out in two steps [122, 126]. The treatment is indicated for immature teeth with necrotic pulps, with or without a periapical lesion. An informed consent must be signed prior to the initiation of the treatment. Other treatment options must be presented, including apexification or extraction of the tooth. It is compulsory to explain that the outcome of the treatment is not predictable, and although apical repair is expected in most cases, the exact outcome may vary [127]. This will be later described in further detail.

17.5.1 Clinical Procedure

The AAE and the ESE published guidelines to regenerative endodontic treatment [126, 128]. The following procedure is based on these guidelines.

17.5.1.1 First Visit

Anesthesia of the tooth is optional, since the tooth is not vital, although patient's cooperation must be considered. Following rubber dam isolation, the access cavity is prepared, and any necrotic pulp tissue is removed from the root canal space. The canals should be irrigated with 20 mL of sodium hypochlorite 1.5%–3% for 5 min. Lower concentrations of sodium hypochlorite are advised because it is less cytotoxic. It was shown that 6% NaOCl had a negative effect on the differentiation and survival of the stem cells of the apical papilla (SCAP) [129]. Negative pressure irrigation or a side-vented needle positioned 1–2 mm above any vital tissues is used to prevent extrusion of the irrigation solution to the periapical tissues. Mechanical instrumentation of the walls of the canals should be avoided. Following NaOCl irrigation, the canals should be irrigated with 20 mL of saline or 17% EDTA for 5 min. The canals are then dried with paper points. Dressing of the root canals can be done with a slurry of $Ca(OH)_2$ or a triple antibiotic paste (TAP) consisting of metronidazole, ciprofloxacin, and minocycline (Fig. 17.4). The antibiotics should be mixed to a final concentration of 1–5 mg/mL, placed apical to the CEJ. The dressing should be placed at least 1 mm shorter than the canal length as not to injure any remnants of vital apical tissues. It can be introduced into the canals using a lentulo spiral or via syringe.

Since the classic composition of the TAP is associated with crown discoloration [122, 124], caused by the minocycline, a modified antibiotic paste is suggested in esthetic regions, especially in anterior teeth [130, 131]. Minocycline can be replaced by another medicament, such as amoxicillin or clindamycin [128]. Alternatively, a mixture of ciprofloxacin and metronidazole, otherwise termed "double antibiotic paste" (DAP), can be placed in the canals [128]. A leakproof temporary restoration should be placed at the completion of this step [126]. The prudent clinician must verify that there are no known allergies to the antibiotics used.

17.5.1.2 Second Visit

The second appointment is scheduled 1–4 weeks later [126, 128]. If signs or symptoms of infection continue, consider repeated dressing of the canal with the same medicament for additional time or use another antimicrobial agent. The tooth is anesthetized with 3% mepivacaine without a vasoconstrictor and isolated with a rubber dam. Then the canals are irrigated with 20 mL of 17% EDTA for 5 min and dried with paper points. At this point, bleeding is induced by the introduction and rotation of a pre-bent Hedstrom file beyond the apex and irritation of the periapical tissue. The canal is allowed to fill with blood up to 2–3 mm below the cemento-enamel junction. The formation of a blood clot is expected within 15 min. If necessary, a resorbable collagen matrix (e.g., CollaPlug®, Zimmer Dental, Carlsbad CA) is placed on top of the blood clot, the matrix should be allowed to soak with the liquid to avoid the formation of a hollow space.

An intracanal non-staining hydraulic silicate cement, for example, Biodentine™ or EndoSequence root repair material, is placed on top of the matrix in a layer of

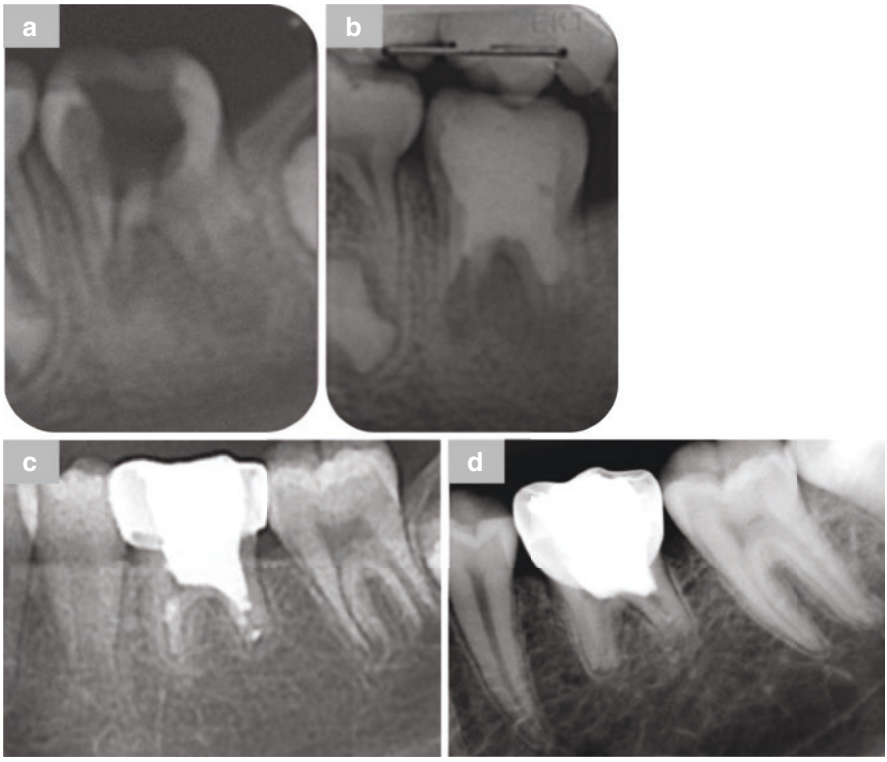

Fig. 17.4 Revascularization with MTA. (Courtesy: Dr. Iris Slutzky-Goldberg). (**a**) A 6.5-year-old girl. Carious first mandibular molar. The access cavity is open to the oral cavity. Previous trials to treat the tooth failed due to poor cooperation. Preoperative demonstrated an immature tooth (Nolla stage 7) with a large periapical radiolucency. (**b**) Post-op radiograph—revascularization under N2O sedation was carried out in two steps: initial dressing with triple antibiotic paste and placement of MTA 4 weeks later on top of the blood clot. (**c**) 5 years' follow-up—the tooth was restored with a stainless-steel crown. Complete healing of the periapical lesion and continued root development. Part of the MTA plug in the both roots dissolved with time. Remnants of the MTA can be seen along the canals. The tooth does not respond to cold tests. (**d**) 12 years' follow-up—normal periapical tissues, continued root development is evident

2–3 mm kept underneath the cemento-enamel junction. The collagen matrix facilitates control of the hydraulic cement that is placed coronally.

Finally, the tooth is hermetically sealed with a glass ionomer (e.g., Fuji IX™, GC America, Alsip, IL) or an adhesive restoration, depending on the type of hydraulic cement used. As previously mentioned, concerns have been raised regarding the strength of the bond between Biodentine™ and glass ionomer or composite [110, 132]. We suggest that an alternative temporary filling material will be placed, until the Biodentine™ has completely set.

17.5.2 Scaffold

The early study of Thibodeau et al. demonstrated better treatment outcome after revascularization in dogs' teeth when a blood clot was present in the apical portion of the disinfected root canals [133]. According to Lovelace, the influx of apical blood into the root canal space was accompanied by an accumulation of undifferentiated mesenchymal stem cells. These cells may promote the regeneration of pulpal tissues. Although the exact source of these cells is not clear, the apical papilla which is rich in mesenchymal cells may be the source [134]. However, bleeding into the root canal space is not always feasible. Several options were suggested to promote bleeding, including the use of an anesthetic solution without adrenalin, as previously described. Alternatively, the use of different scaffolds, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), was suggested in regenerative endodontic treatment [135].

The outcome of endodontic regeneration using blood clot induction (BC), PRP, and PRF in revascularization of immature necrotic teeth was compared 1 year after completion of the treatment. PRP was better than PRF or BC when the periapical healing was evaluated. Elongation of the root, thickening of the dentinal walls, and response to vitality testing was similar among groups [136].

In contrast, the results of revascularization using induced platelet pellet (PP) without prior apical bleeding, BC, PRP, and PRF were compared in another in vivo study. The procedure was performed in 88 immature necrotic incisor teeth in children aged 8–11. After 28 months' follow-up, an apical root closure was observed in 73.9% of the teeth, usually in a conical shape, with similar closure rates among groups. Nevertheless, the radiographic root area, corresponding to the extent of root development of the BC, was significantly greater than those of the PP and PRF groups. The radiographic canal area in the BC group was significantly greater in comparison to the other scaffolds used. Clinically 86% of the teeth were positive to sensitivity testing [137]. However the use of PRP or PRF requires drawing of blood from the patient and handling of the blood, thus making the procedure more cumbersome, and requires patient's cooperation which may be problematic especially in apprehensive children.

17.5.3 Follow-Up

Follow-up is scheduled for 6 months, a year, and then yearly after revascularization [126, 128].

17.5.4 Expected Outcome

Primary goal: Resolution of the periapical lesion and elimination of symptoms (Fig. 17.4).

Secondary goal: Continued root maturation, including an increase of root wall thickness and elongation of the root. This may occur within 1–2 years after treatment.

Tertiary goal: Positive response to sensibility testing (AAE).

It is noteworthy that the outcome of revascularization is influenced by many factors, such as patients' age, apical diameter, the type of dressing material, the scaffold, the capping material, and the follow-up period. Thus, making a comparison between the different protocols is very difficult, especially with the lack of enough available data.

17.5.4.1 Healing of Periapical Lesions

Periapical healing after revascularization is expected in most of the cases. The reported healing rate of periapical lesions in immature teeth is relatively high ranging between 93% [138] and 100% [139, 140].

17.5.4.2 Continued Root Maturation

Ong et al. in a meta-analysis published in 2020 concluded that although root thickening occurred in 90.6% of the cases, lengthening of the root was observed in only 77.3% of the cases, and the incidence of apical closure was 79.1%. However, if a cutoff point of 20% radiographic change, representing a more significant clinical change, was used, then regenerative endodontics would have resulted in only 39.8% root thickening and 16.1% elongation [138].

17.5.4.3 Response to Sensibility Tests

Doubts have been raised as to the positive response of the revascularized teeth to the application of thermal tests such as Endo Ice and other refrigerating materials or EPT, especially considering the intracanal MTA or bioceramic barrier. Saoud et al. reported the successful outcome of revascularization in 20 traumatized immature permanent necrotic teeth, although none of them regained their responsiveness to sensibility testing [141].

17.5.5 Survival

High survival rates were reported. A longitudinal cohort study of regenerative endodontic treatment of immature necrotic teeth found survival rate of 96.4% [140]. The Mahidol study reported a 100% survival rate [139], whereas a systematic review and meta-analysis based on three randomized controlled trials, six prospective cohort studies, and two retrospective cohort studies reported 97.3% survival [138]. Similar survival rates (96%) were reported by Wikstrom et al. in a systematic review that included only peer-reviewed studies of at least 20 cases followed for 2 years [142].

17.5.6 Pulp Regeneration

Regeneration, which is expected to take place after a revitalization procedure, refers to the restoration of the original tissue function and architecture. Pulp-like tissue formation within the root canals is expected where stem cells will differentiate into odontoblasts capable of secreting tubular dentin [143]. The early study of Thibodeau in dogs (2007) demonstrated continued root development. Histologic evidence of hard tissue formation was observed in some of the cases, with new vital tissue in the canals [133], although these tissues lack the characteristics of a normal dentin-pulp complex.

There are no human studies regarding the nature of tissue forming in the root canals. Our knowledge is therefore based on animal studies or case reports. In an animal model, canines from four ferrets were infected, dressed with TAP, and then used either BC or PRP as a scaffold. Ingrowth of hard tissue was observed in the apical part of the root canal [144]. In a study which used dog's teeth, vital tissue formed in the canal space of 30 premolars treated by revascularization. The teeth were treated by either TAP, Propolis, or without any medication. The new tissue found in the canals had characteristics of cementum and PDL [145]. Saoud et al. demonstrated that the tissue found in the root canals of Mongrel dogs was cementum-like, bone-like, and periodontal ligament-like, and in some cases ingrowth of apical bone into the root canals was observed [146].

Shimizu et al. in a case report examined the tissue formed in a human immature permanent tooth after revitalization. The procedure was considered successful, and continued root maturation was observed. The tooth was extracted 26 months after treatment because of an unrestorable horizontal crown fracture. The histologic examination revealed well-mineralized cementum- or bone-like tissue [147]. Becerra et al. examined the tissue formed after revascularization in a tooth that was extracted because of orthodontic reasons. The radiographic examination showed resolution of the apical radiolucency and narrowing of the root apex. The histologic examination demonstrated soft connective tissue similar to that in the periodontal ligament and cementum-like or bone-like hard tissue [148]. Martin et al. examined the histologic characteristics of a fractured extracted molar 2 years after revascularization using PRF. They could not find any pulp-like tissue or the presence of polarized odontoblasts along the dentin. The irregular mineralized tissue formed in the distal and mesial canals was cementum-like with an uninflamed fibrous connective tissue that could be followed up to the MTA plug [149].

Based on the currently available data, it can be concluded that true pulp-dentin complex regeneration does not occur as a result of this treatment. Therefore, a more appropriate way to describe the outcome of the procedure is revitalization or revascularization.

17.5.7 Tissue Reactions

Chen et al. described the outcome of revascularization in 20 immature necrotic permanent human teeth diagnosed with either apical periodontitis or apical abscess [127]. The patients were followed up from 6 to 26 months. Although ideally continued root maturation and apical root closure is expected after revascularization, described as type 1, this result is not predictable. Four additional types of radiographic responses to the revascularization procedures were also observed: type 2, the root apex becoming blunt and closed, without any significant continuation of root development; type 3, continued root development, although the apical foramen remains open; type 4, severe pulp canal obliteration (Fig. 17.4); and type 5, a hard tissue barrier formed in the canal apical to the coronal MTA plug [127]. Chan et al. followed 28 teeth after revascularization for 30 months. According to their study, complete apical closure was radiographically observed in only 30.8% [140]. Fida et al. reported radiographic evidence of bone ingrowth into the root canal space in three cases. The bone was surrounded by normal PDL without ankylosis [150].

17.5.8 Influence of Apical Diameter on the Outcome of Revascularization

An apical foramen size of 1.1 mm was thought to be necessary for successful revascularization [151]. However successful revascularization cases were observed even when the diameter was as small as 0.5 mm. A study compared the outcome among two age groups: children aged 9–13 and 13–18. The authors found that after a 12-month follow-up period, the younger group showed significant increase in root length and width of the canal walls (Fig. 17.4). However, in the group of children aged between 13 and 18, a wider diameter (larger than 1 mm) resulted in greater increase in root length and thickness. They stated that the preoperative apical diameter is a strong predictor for the outcome of the procedure [152]. The longitudinal study by Chan et al. [140] previously described concluded that teeth with more immature stages of root development had a higher percentage of change in root thickness, length, and apical diameter. The authors of the study used a triple antibiotic mixture, consisting of cefaclor, ciprofloxacin, and metronidazole. Furthermore, this change was more evident in teeth with less than half of the root length formed than in teeth with the root almost completed with an open apex (Nolla stage 9) [153].

Considering the data presented, we suggest that the less developed the root, the more advantageous a revitalization would be. Alternatively, root canal treatment including apexification (apical plug) can be considered for the treatment of teeth with an open apex with an inflamed or necrotic pulp. This will be discussed later in this chapter.

17.5.9 Comparison of Revascularization and Apexification

The Mahidol study compared the outcome of calcium hydroxide apexification, MTA apexification, and revascularization in immature necrotic teeth. The survival rate of revascularization (100%) was similar to MTA apexification (95%) but significantly higher than calcium hydroxide apexification (77%). The study also demonstrated similar success rates for the three treatment modalities [139].

A meta-analysis published in 2019 showed no statistical difference between the overall clinical and radiographic outcome of revascularization using blood clot induction or MTA apexification. Similar survival rates were also reported. The authors reviewed 231 papers although only four papers were included [154]. Wikstrom et al. in 2021 evaluated in a systematic review the survival, success, and root development after regenerative endodontics or MTA apexification of immature necrotic teeth. According to their review, both treatments were effective and had equal success and survival rates. However, endodontic regenerative techniques were superior to apexification in terms of continued root development [142].

Based on the data presented, we recommend that revascularization/revitalization will be performed in immature necrotic teeth with an early stage of root development. Teeth with an apical diameter larger than 1 mm are good candidates for this procedure in all age groups. Revascularization offers a potential for root elongation and thickening of the canal walls and is more effective in less mature teeth. Over time it is, therefore, more advantageous in teeth with unfavorable crown:root ratio. Furthermore, if revascularization fails, a second option for a conservative root apexification is available [154]. On the other hand, if the root has almost reached its full development, apexification and root filling have a more predictable outcome. It should be emphasized that although revascularization enables root apexogenesis, it has no effect on strengthening the peri-cervical area which is more prone to fractures in young permanent teeth.

17.6 Root Canal Treatment in Young Permanent Teeth and Apexification

Root canal treatment in young permanent teeth should be the last option for treatment and performed only when other vital pulp treatment options are not possible or when the diagnosis of pulp necrosis is conclusive [119].

It should be noted that in many cases root canal treatment may be much more complicated than initially thought, because of the specific characteristics of these teeth and the cooperation of the young patient. Vital pulp therapy is easier to perform, more conservative, and more cost-effective [155] (Fig. 17.4a).

Dental caries and traumatic injuries are the most common problems leading to pulp necrosis in children with young permanent teeth [53]. In the carious tooth, the immune responses develop as the lesion advances, leading to increased inflammation, edema, and pain. Eventually, the inflammation in the low compliance environment of the pulp space will cause pulp disintegration and apical pathosis [156].

The development of the root is completed approximately 3 years after eruption [1]. The root morphology and the degree of apical closure vary in accordance with the stage of root development. Root canal treatment in immature young permanent teeth creates distinct problems in disinfection, obturation, and badly broken-down teeth also in restoration. Thinner canal walls and more immature and wider apical foramen make the treatment more challenging. These teeth are also more susceptible to root fracture after treatment [11, 157].

In a retrospective cohort study published in 2021, the estimated 5-year survival rate of 424 endodontically treated teeth was 80% for 15–18-year-olds, 64.8% for 12–14-year-olds, and 46.4% for 6–11-year-olds. In the total study sample, the estimated cumulative survival probability was 69.1% at 5 years. The authors concluded that endodontically treated teeth are more likely to survive when the treatments are performed at an older age [158].

17.6.1 Clinical Procedure

Conventional root canal treatment includes access preparation, cleaning, shaping, disinfection (chemical and mechanical preparation), and obturation of the canal system followed by restoration of the treated crown [128].

Before treatment, a careful radiographic evaluation of the roots and pulpal anatomy is indicated, using one or two radiographs from different horizontal angles. The use of a vertical bitewing radiograph can allow visualization of the extent of carious damage, the furcation area, and the height of marginal bone. In young children with shorter roots, it can also demonstrate the periapical area, making a second periapical radiograph unnecessary.

The use of CBCT may be essential in complex cases [50, 159] (see radiographic examination). The use of magnification (preferably a dental operating microscope) and illumination during the treatment is recommended.

17.6.1.1 Access Preparation

Following anesthesia, the tooth is isolated with a rubber dam. This may be extremely challenging in the erupting tooth. Several options are suggested: including the placement of the clamp on a posterior tooth, gingivectomy to expose the cervical region, use of a serrated clamp, or placement of the sterile clamp on the gums. When there is a risk of complex anatomy (e.g., dense invaginatus, calcifications, etc.) of the tooth, rubber dam placement can be postponed after the initial or complete access preparation.

Before entering the pulp chamber, all caries should be removed and preferably all present crown restorations. During access preparation, the entire roof of the pulp chamber and all coronal pulp tissue (vital or necrotic) is completely removed; special care must be taken to any pulp tissue in the pulp horns. Sound tooth structure should be conserved as much as possible.

The pulp chamber is rinsed throughout the preparation with NaOCl, and all the canal orifices are located [160].

17.6.1.2 Mechanical and Chemical Preparation

The mechanical and chemical preparation is aimed to disinfect the canal system to prevent any periapical disease or promote healing and repair of the peri-radicular tissues [128]. The mechanical preparation objectives are to remove infected hard and soft tissue, allow access to disinfecting irrigants to the entire canal space, and create space for the delivery of medicaments and obturation materials while retaining the integrity of radicular structures [160]. After locating the canal orifices, the canal length is estimated with a parallel preoperative radiograph. The canal length is measured using an electronic apex locator (EAL) and confirmed with a radiograph. It should be taken into consideration that EAL measurement can be inaccurate in canals with open apices.

In these cases, final confirmation using paper points is possible. The paper point is inserted briefly 2 mm short of the approximated canal length and after withdrawal inspected for moisture at the tip. When the tip is dry, this action is repeated in increments, each time 0.5 mm longer. The working length is at the point in which moisture is present [161].

The mechanical preparation includes the use of hand and rotary nickel-titanium (NiTi) files. In immature teeth with wide or blunderbuss canals, this preparation is not effective as the files will not contact the entire canal walls. In narrower canals, rotary NiTi files are recommended, as they better follow the original morphology of the canals and reduce preparation errors [160]. Filing should be cautious because it can endanger the thin dentinal walls. Additionally, the use of non-standardized files, such as XP finisher (FKG, Switzerland) or SAF (ReDentNova, Israel), can aid in the preparation of the wide canals.

During the mechanical preparation, the canal is irrigated with a disinfecting irrigation solution. The most common solution is NaOCl because of its antimicrobial and tissue (necrotic and vital) dissolving properties (see Sect. 17.3).

Care should be taken not to extrude the solution beyond the wide apical foramen. Therefore, in young permanent teeth, the use of a lower concentration of NaOCl should be considered. Copious amounts of irrigation solution should be used to compensate for the low concentration [162]. Irrigation needle with a blunt end and side vented holes should be placed passively 1 mm short of the canal length [163]. Passive ultrasonic irrigation can also be useful in the canals of immature teeth [164, 165]. The use of negative pressure irrigation system, e.g., EndoVac (Discus Dental, Culver City, CA) is recommended for effective and safe irrigation [166].

Ethylenediaminetetraacetic acid (EDTA) is a chelating agent and can be used in a concentration of 17% to irrigate the canal before final rinsing with NaOCl to remove the smear layer [167] (see Sect. 17.3).

The use of 2% chlorhexidine (CHX) instead of, or in combination with, NaOCl is also possible as it has lower cytotoxicity. Nevertheless, although the materials have the same antimicrobial properties, CHX has no tissue-dissolving properties [55].

When the root canal treatment cannot be completed in one appointment, $Ca(OH)_2$ is used as an intracanal medication. Although recent studies suggest that there is no difference in the outcome of root canal treatment in one versus multiple visits [168], dressing the canals in immature permanent teeth with $Ca(OH)_2$ can be beneficial, as

the removal of tissue remnants and disinfection can be compromised especially in very young roots [169]. When the canal preparation is complete, a lentulo spiral is used to deliver a creamy mix of $Ca(OH)_2$ into the canal. The canal is medicated for at least 1 week for additional disinfection [170].

17.6.1.3 Root Canal Obturation

Obturation of the canal system is performed after disinfection is completed. In young permanent teeth filling, the root canal can be difficult as the open apex provides no barrier for the root filling material. Moreover, the canals are usually divergent, and the apical diameter of the canal is larger than the coronal diameter, thus compromising the control of the obturation material in the apical area. Furthermore, forces applied on walls in some obturation techniques can endanger their integrity and lead to fractures [11]. Following rubber dam isolation, the canals are irrigated with 17% EDTA to remove the $Ca(OH)_2$ and then irrigated with NaOCl. The canals are then dried with paper points and the appropriate obturation technique should be chosen according to the apical morphology.

Root Canal Apexification in Immature Roots: Apical Barrier Technique

At this point, an exact assessment of the size of the apical foramen and the shape of the apical portion of the canal is made. Traditionally, apexification was performed in roots with a wide or divergent apex. This included the placement of long-term calcium hydroxide dressing in the canals to induce a calcified barrier formation [171]. The time required for apical barrier formation may be as long as 6–24 months [65] and requires the patient's compliance. Furthermore, dressing the tooth with $Ca(OH)_2$ for a long period is associated with a decrease in fracture strength of immature roots [172]. In another study, dressing dentin with $Ca(OH)_2$ for 30 days reduced the compressive strength of dentin, irrespective of the vehicle use: normal saline, distilled water, or a local anesthetic solution [173].

A simple and less time-consuming procedure is the apical barrier technique, which involves the placement of a barrier at the apical region to prevent extrusion of filling material (AAE 2019). This can be done by placing a minimum layer of 3–4 mm of MTA or a bioceramic material at the apical foramen [11], 1 mm short of the radiographic apex (Fig. 17.5b). Introducing a resorbable collagen matrix (e.g., CollaPlug®, Zimmer Dental, Carlsbad, CA) apical to the MTA or bioceramic material can aid in controlling the material [174]. In our opinion, materials having putty consistency (e.g., Biodentine or EndoSequence root repair material) are more user-friendly. The remaining space of the canal is filled in the next step using gutta-percha and a sealer (see below) (Fig. 17.5c).

Obturation of Mature Roots with Open Apices

An endodontic sealer is introduced into the dry canals. A gutta-percha master cone fitted to the working length is placed in the canal and the canal is obturated using lateral condensation, warm obturation, or a combined technique. The use of warm GP should be avoided when there is a risk of extrusion of the obturation materials beyond the apical foramen, thus irritating the periapical tissues.

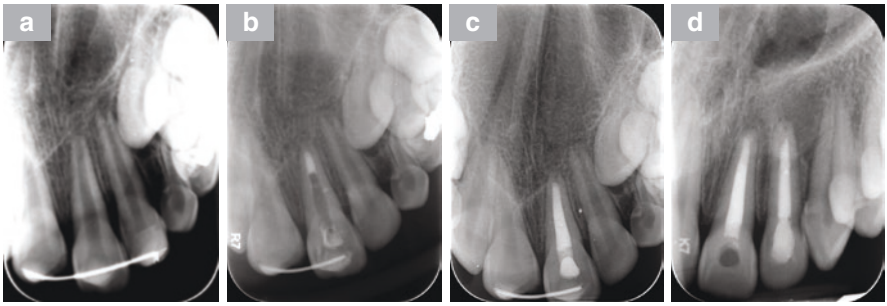

Fig. 17.5 One visit apexification and root canal treatment. (Courtesy: Dr. Iris Slutzky-Goldberg). (**a**) An 8.5-year-old girl. Left central incisor 3 weeks after extrusion and splinting. Negative response to sensibility testing and stage II mobility (despite the splint). No pain was present during test cavity preparation, which revealed a necrotic pulp. Since the root was almost fully developed, root canal treatment was initiated. (**b**) A 3 mm apical barrier with EndoSequence root repair material. Due to increased mobility, a splint was left in situ. (**c**) Root canal obturation with gutta-percha and AH plus root canal sealer. The splint was removed after the procedure. (**d**) 4 years' follow-up—the tooth presents no signs or symptoms. The lateral incisor was treated due to the diagnosis of apical periodontitis

In wide canals, the canal can be obturated using the chloroform dip technique. This technique enables better control and adaptation of the cone to the shape of the apical portion of the canal and therefore simplifies the obturation process. The use of chloroform has been gradually minimized due to concerns as to its toxicity and carcinogenicity and replaced by other solvents (e.g., eucalyptol) A master gutta-percha point is fitted with friction resistance few millimeters short of the working length. The tip of the cone is dipped in the solvent or heated for 1–2 s to soften only the outer superficial layer of the gutta-percha. The softened cone is inserted repeatedly into the canal until the cone reaches the working length and an impression of the apical portion of the canal is obtained. The position and fitness of the cone are verified with a radiograph [175]. The canal is then obturated using a sealer and the customized cone in the chosen obturation technique.

The use of recently introduced calcium silicate-based sealers can be considered in root canal obturation of immature permanent teeth. The properties of some of these sealers have been published and reported to be similar to MTA. They are considered bioactive (promoting cell proliferation and adhesion, stimulate hard tissue formation), biocompatible, and hydrophilic [176]. A recent review states that their main advantage is their bioactivity and their ability to stimulate hard tissue formation [177]. However, more investigation of these materials is recommended, and the clinician is advised to review the research published in the endodontic literature.

The calcium silicate-based sealer is delivered into the canals system by a lentulo spiral, a special flexible plastic tip, or the gutta-percha master (primary) cone. A single fitted master cone is then inserted into the canal; additional compaction is not mandatory. This technique allows adaptation of the sealer to the irregular canal, enables better control of the obturation material at the working length, and does not risk the thin canal walls, as no forces are applied during the obturation.

17.6.1.4 Coronal Restoration

The restoration of the crown of an endodontically treated tooth is of utmost importance. An adequate root canal treatment and adequate crown restoration will increase the probability of healing of apical periodontitis [178]. Coronal restoration should restore the tooth's esthetic and function while protecting the residual tooth structure, especially in immature permanent teeth that are prone to fracture [11]. The European Society of Endodontology (ESE) published in 2021 a position statement regarding the restoration of root-filled teeth [179]. It recommends that premolars and molars should be restored with cuspal coverage restorations when at least one proximal wall is missing while retaining as much sound tooth structure as possible. This type of restoration is also indicated when a crack is visible. Anterior immature endodontically treated teeth have thin dentinal walls that are more susceptible to fracture especially in the cervical area (particularly as a result of trauma) [180]. In these cases, an intra-coronal bonded restoration is recommended after the removal of the root filling material below the marginal bone level in an attempt to reinforce the tooth structure [181, 182].

In anterior and premolar teeth "passive" post placement is beneficial when no remaining coronal dentin walls are present. In order to preserve sound tooth structure, an endocrown can be considered as an appropriate alternative to conventional full-coverage stainless-steel crown [183] (details in Chap. 18).

17.6.1.5 Follow-Up

Follow-up appointments should be scheduled regularly to assess the treatment outcome. Clinically no adverse signs and symptoms are detected, and the crown is sealed with a good restoration that does not allow coronal leakage. Radiographic evidence of resolution of periapical pretreatment periodontitis or normal periapical tissue is observed with no additional breakdown of the periodontal supporting tissues [119].

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Restoring the Endodontically Treated Young Permanent Tooth

18

Zafer C. Çehreli

Contents

18.1 Introduction

A young permanent tooth may occasionally require vital or nonvital endodontic therapy as a consequence of dental caries or trauma. For decades, it was believed that the effectiveness of root canal treatment was influenced by the technical quality of the root filling [1]. Today, there appears to be ample evidence that the success of endodontic therapy is equally [2] or even more affected [3–5] by the quality of the coronal restoration than the technical quality of the endodontic therapy itself. Thus, it is important for the pediatric dentist to know that in addition to restoring the function and esthetics, a post-endodontic restoration should safeguard the endodontically compromised tooth by preventing coronal microleakage and minimizing oral fluid and bacterial leakage into the periradicular space. Based on limited evidence, the best way to restore a tooth after endodontic treatment remains a controversial topic for young permanent teeth. This chapter will review conventional and emerging treatment options for the restoration of endodontically treated young permanent teeth along with the factors associated with the long-term survival.

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18.2 The Access Cavity

The endodontic treatment of immature permanent teeth with necrotic pulps involves little to no mechanical instrumentation so as to preserve the existing thin root walls. Instead, the root canal is thoroughly disinfected in a non-instrumental fashion by using large amounts of sodium hypochlorite (NaOCl) with a long contact time. NaOCl, the most effective antibacterial irrigant in endodontics, has a low molecular weight along with the ability to penetrate both the dentinal tubules and the intricate morphology of the root canal system, making it more effective than any endodontic metal instrument at removing the infected material. It could even be argued that the new root canal tool in endodontics is a liquid—not metal—which just so happens to be NaOCl, thanks to recent advancements in active and closed irrigation systems using exclusively NaOCl and our long-term learning experience from the non-instrumental root canal disinfection procedures of regenerative endodontics. It is crucial to understand that each and every infected dentinal tubule is a root canal system in and of itself and that the treatment of infected dentinal tubules necessitates the use of liquids and flowable materials for everything from cleaning to sealing.

Because NaOCl selectively removes the organic component of dentin, particularly type I collagen which is necessary for micromechanical retention of dentin bonding agents, exposing the pulp chamber to extended contact with NaOCl might have a negative impact on the effectiveness of resin adhesion [6]. Removal of the superficial collagen network by NaOCl also weakens the mechanical and structural properties of dentin [7], leading to decreased fracture strength [8], which might pose a serious concern in an already fracture-prone immature permanent tooth. This potential problem can be managed practically by avoiding high concentrations of NaOCl for irrigation [8].

Always and unavoidably, endodontic sealers contaminate the endodontic access cavity. While there is currently no method that can entirely remove sealer residue from cavity walls, traditional alcohol cleaning still appears to be the most efficient and practical way to remove sealers to the best extent, compared to bur cleaning or particle abrasion [9], with no additional benefit of combining the latter two methods with alcohol cleaning. The European Society of Endodontology recommends cleaning of the cavity walls with a diamond bur or air abrasion with aluminum oxide to remove the MTA or tri-calcium silicate cement contamination on access cavity walls [10].

Ideally, the endodontic access cavity and the crown should be restored at the same visit with root canal filling. In the case of an indirect restoration requiring multiple visits, the endodontic access cavity and surrounding restoration margins/surfaces must be adhesively sealed immediately after root canal obturation, before impression taking. Delaying the coronal restoration with a temporary material for extended periods increases the likelihood of recontamination of the root system as well as risk of future fracture.

18.3 Intraorifice Barrier

In order to decrease coronal microleakage in root-filled teeth, the intraorifice barrier concept has been proposed [11]. This simple-yet-effective procedure involves replacing 3 mm of gutta-percha at the orifice of the root canal with a restorative material (Fig. 18.1). Numerous investigations have shown the positive impact of intracoronal barriers in successfully preventing or reducing coronal microleakage, depending on the material used [12, 13]. More recently, it was demonstrated that root-filled teeth with an intraorifice barrier are more resistant to post-endodontic root fractures than those without one [14]. Thus, routine placement of intraorifice barriers may be a useful reinforcement in young permanent incisors that have undergone endodontic treatment when full coverage restorations with the known ability to reduce root fractures cannot be used. Bonded resin composites, resin-modified glass ionomer cements, and fiber-reinforced composites are commonly used as intraorifice barriers. In vitro testing has shown that calcium silicate-based materials employed as coronal barriers in regenerative endodontic procedures also function as intraorifice barriers and have a significant sealing and strengthening effect [14].

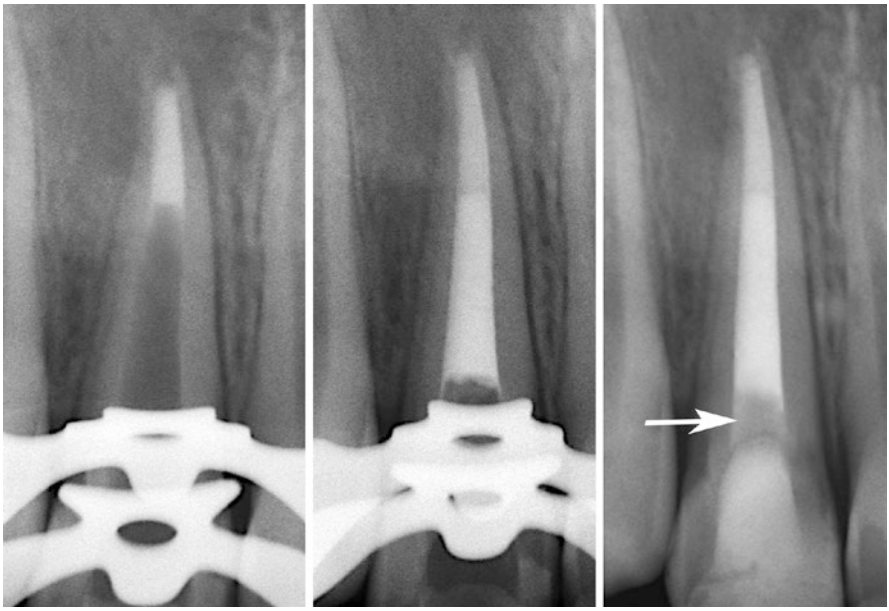

Fig. 18.1 Radiographic view of a resin-modified glass ionomer intraorifice barrier placed over a root canal filling with mineral trioxide aggregate apical barrier in a young permanent incisor (arrow). (Courtesy of Dr. H. Simsek & Dr. Z. Cehreli)

18.4 Coronal Restoration of Endodontically Treated Young Permanent Teeth

Endodontically treated teeth undergo a number of irreversible structural changes, including dentinal dehydration, changes in dentin collagen composition, and a reduction in micro-hardness, which all may be linked to the risk of future fracture [15]. When combined with extensive tooth structure loss, root-filled teeth typically need massive partial or full coverage restorations to sustain the remaining tooth structure. The evidence base for the restoration of posterior teeth indicates that modern indirect procedures such as onlays and endocrowns are as predictable as full coverage crowns.

18.4.1 Young Permanent Molars

18.4.1.1 Prefabricated Crowns

Prefabricated permanent molar crowns (also referred to as adult stainless-steel crowns) have an overall success rate of almost 90% and an average longevity of about 45 months across all age categories, with particularly good results in patients under the age of 9 [16]. The American Academy of Pediatric Dentistry recommends using adult prefabricated crowns as a semi-permanent restorative option for the management of immature permanent molars with severe enamel defects or considerable carious tissue loss [17]. When esthetics is not an issue, permanent molar steel crowns may be the most reasonable, cost-effective restorative option in endodontically treated, severely broken-down young permanent molars. In molars with a smaller crown size, oversized primary stainless-steel crowns may be utilized as an alternative to permanent molar crowns. Adult preformed crowns do not replace the need for permanent restorations in the future.

There is currently no clinical evidence to support the long-term effectiveness of newly introduced permanent molar zirconia crowns. Based on the literature from primary zirconia crowns, the American Academy of Pediatric Dentistry [17] has reported that the use of zirconia crowns may be associated with better gingival health than stainless-steel crowns [18] (Fig. 18.2).

18.4.1.2 Indirect Restorations

Today, there is convincing evidence that molars and premolars with sufficient depth and form within the pulp chamber for core retention can be safely restored without the use of post systems [19]. Endocrown, a minimally invasive restorative treatment option, has been utilized effectively in the adult population as an alternative to the standard post and core technique for over two decades [20]. Endocrown can be defined as a monoblock adhesive restoration that consists of a crown and pulpal extension that is bonded to the pulp chamber and cavity margins of an endodontically treated tooth. Because post space and ferrule are preparation that are eliminated with the use of endocrowns, the remaining tooth structure can be preserved. Along with the advances in the computer-aided design and manufacturing

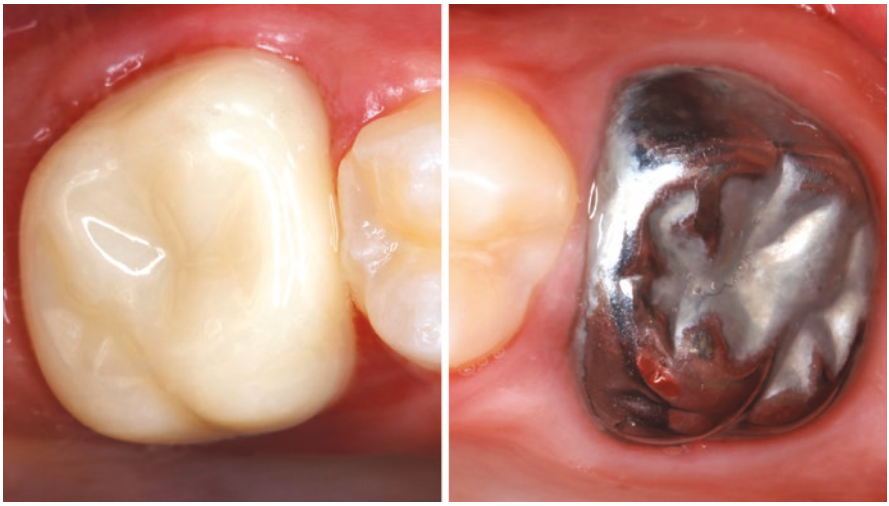

Fig. 18.2 Visible plaque accumulation and marginal gingival view of adult stainless-steel crown and zirconia crown in the root-filled molars of the same patient after 18 months of clinical use. (Courtesy of Dr. Z. Cehreli)

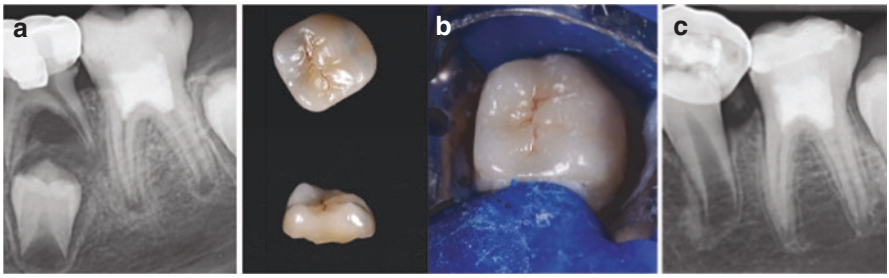

Fig. 18.3 (**a**) Postoperative radiographic view of a structurally compromised, MIH-affected permanent first molar after cervical pulpotomy with a calcium silicate-based material. (**b**) Placement of the lithium disilicate CAD/CAM endocrown under strict isolation. (**c**) 2-year follow-up, demonstrating complete root development in the absence of periapical pathosis. (Courtesy of Dr. E. Nuni, Dr. E. Davidovich)

(CAD-CAM) process and resin composite materials, the use of CAD-CAM endocrowns in young permanent teeth has become a viable esthetic alternative to adult stainless-steel crowns (Fig. 18.3). The CAD-CAM technique uses intraoral scanners to obtain digital impressions, which offers a distinct benefit over the difficult traditional impression taking method in youngsters with poor cooperation [21]. Endocrowns have shown good long-term survival rates in adult molars and premolars, with considerably less catastrophic failures than post and post-and-core retained coronal restorations [20].

Onlays are another viable esthetic restorative option in root-filled young permanent molars with reduced cuspal support due to extensive carious tissue loss [22].

Onlays, like endocrowns, can be produced from resin composite blocks using a CAD-CAM process, saving chairside time and improving patient compliance. Onlays have shown superior mid-term survival rates in primary molars than stainless-steel crowns [22].

18.4.2 Young Permanent Incisors

Direct, light-cured resin composites should be used for the post-endodontic restoration of young permanent incisors with merely an endodontic access cavity. Because of the presence of surrounding enamel margins, such bonded restorations have excellent long-term sealing capacity and are rarely subjected to masticatory stresses that may cause catastrophic failures.

Based on the traditional approach, it may be assumed that endodontically treated incisors with moderate to extensive tissue loss should ideally be restored with posts to provide retention for the coronal restoration. Indeed, severely compromised immature permanent incisors with large, flared root canals can be practically restored with adhesively luted bundled glass fibers or a combination of bundled glass fibers and conventional solid glass fiber posts to conform to the irregularly shaped canal space [23]. However, in the event of a mesial or mesial and distal class III cavity, as well as an endodontic access cavity, direct resin composite restoration of the root-filled crown has demonstrated to have comparable fracture strength to those restored using bundled and solid post systems [24]. There is even growing evidence that glass fiber posts may not necessarily provide better fracture resistance than a simple, bonded direct composite core buildup, when sufficient coronal dentin (ferrule) is available as an intrinsic reinforcement to the core [25–27] (Fig. 18.4). More importantly, the use of a fiber post cannot compensate for the absence of a ferrule [26]. Thus, in endodontically treated young permanent incisors, it seems reasonable to follow the no-post approach performed by the use of bonded direct composite build-up, so as to decrease the likelihood of unrestorable failures.

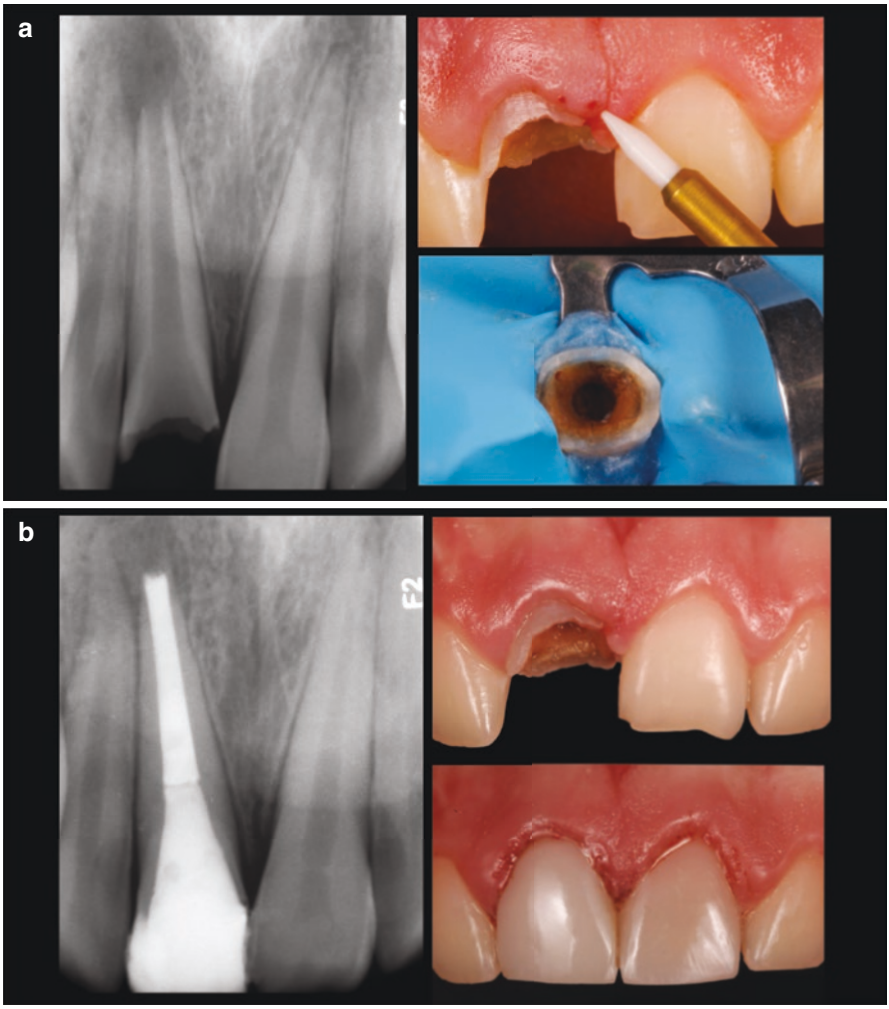

Fig. 18.4 No-post approach in a severe crown fracture. (**a**) Preoperative radiographic view, followed by crown lengthening with ceramic bur and endodontic treatment under isolation. (**b**) Root canal filling with final coronal restoration made by bonded direct composite buildup. (Courtesy of Dr. Z. Cehreli)

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Elucidating Tooth Development and Pulp Biology by Single-Cell Sequencing Technology

19

Jimmy K. Hu and Amnon Sharir

Contents

19.1 Introduction

This chapter discusses recent advances in using single-cell transcriptomic technology to study tooth development and pulp biology. While the tooth is a mineralized organ, its vitality and function are supported by soft tissues, such as the periodontal tissues and the dental pulp [1, 2]. These tissues contain diverse cell populations that are progressively formed during embryonic development. Decades of research have

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revealed the major cell types that comprise the dental pulp, as well as of some of the genetic and signaling pathways that govern its development and maintenance. These efforts paved the way for research that aims to utilize dental pulp cells as a source of stem cells in regenerative medicine [3].

To identify marker genes for each cell type in the dental pulp, decipher the cellular hierarchy, and decode the functions of identified genes and pathways, early experimental approaches examined dental cell populations in bulk. However, the lack of cellular resolution has limited our capacity to deconstruct the heterogeneity within each cell type and the regulatory interactions between subpopulations during development and regeneration. The advent of single-cell transcriptomic technology has truly revolutionized biological studies and, particularly, dental research. This approach allows interrogation of gene expression in each cell of a complex tissue and, thereby, the discovery of inherent cell lineages, interactions, and transcriptional controls. In this chapter, we present recent benchmark single-cell studies that addressed key questions in tooth development and highlight findings that advance our understanding of how the dental pulp forms and functions.

19.1.1 Clinical Relevance, Challenges, and Questions

The dental pulp is the inner soft tissue of the tooth that is surrounded by the hard mineralized structures of enamel and dentin. Composed of connective tissues, vasculatures, immune cells, nerves, and the dentin-producing odontoblasts, the dental pulp plays indispensable roles in tooth homeostasis and is thereby essential for the vitality of the tooth. Although protected externally, the dental pulp can incur injuries and inflammations due to trauma, tooth decay, and cavities. Having only a limited capacity for self-repair, the standard treatment of pulp diseases often involves root canal therapy, where soft tissues are removed and then replaced by inorganic materials. This, however, deprives the tooth from natural blood and nervous supplies, hence making the tooth susceptible to structural failures and re-infections [4]. By contrast, regenerative strategies using mesenchymal stem cells (MSCs) or dental pulp stem cells (DPSCs) hold promise to restore the natural biological functions of the dental pulp.

Despite promising advances in stem cell-based pulp regeneration in both preclinical and clinical settings, applications of these strategies remain limited in dentistry today [5, 6] due to several translational hurdles. First, we lack reliable markers for the numerous sub-populations of the heterogeneous pulp tissue, as well as sufficient knowledge about the differentiation potential of each sub-population. This has hindered the efforts to isolate the correct populations for specific clinical applications. Second, our understanding of the genetic and signaling mechanisms that control the differentiation processes during pulp development are limited. Therefore, it is currently challenging to control the proliferation and differentiation of dental pulp stem cells toward a desired fate, let alone to produce the different lineages that will reconstruct the cellular compositions and architecture of pulp. Lastly, there is

little knowledge about the signals required to maintain stem cell survival and function in teeth or in the engineered niche after transplantation.

In recent years, single-cell RNA sequencing (scRNA-seq) studies have begun to address some of these issues by providing insights into the complexity of cellular compositions in the developing pulp and by uncovering the dynamic differentiation processes through which dental progenitors give rise to diverse tooth cell types. These studies also revealed key gene regulatory networks that drive the specification of each cell type, as well as the dominant signaling interactions that contribute to the regulation of pulp development.

19.1.2 Tooth and Pulp Development

Chapter 1 explains in detail the developmental processes of tooth and pulp formation. Here we emphasize key events that will be discussed in the context of single-cell transcriptomics in later sections. Akin to other organs in the vertebrate mouth cavity, the tooth develops from the first pharyngeal arch that encompass both the mandibular and maxillary processes. In humans, pharyngeal arches are formed around the fourth week of development, while in mice they first become apparent around embryonic day (E) 8.5. Much like an apple with a thin layer of skin, the pharyngeal arch comprises a bulk of mesenchymal cells that are ensheathed by a continuous epithelial layer of ectodermal and endodermal origins [7]. The ectoderm overlays the outer arch, while the endoderm coats the inner surface. The mesenchymal cells also have dual origins. Whereas the core contains cranial mesoderm that gives rise to most of the head muscles, the rest of the mesenchyme is derived from cranial neural crest cells with broad fate potential. Unlike mesodermal cells, the cranial neural crest is derived from the ectoderm through a process known as epithelial-to-mesenchymal transition (EMT). In this process, some ectodermal cells, also known as ectomesenchyme, delaminate from the ectodermal epithelium in response to Wnt and Fgf signals and migrate to populate the forming pharyngeal arches [8–10]. In the cranial region, EMT occurs prior to the neural fold closure and the ectomesenchyme arises from a group of E-cadherin-expressing non-neural ectodermal cells lateral to the N-cadherin-expressing neural ectoderm [11, 12] (Fig. 19.1a). Subsequently, ectomesenchyme gives rise to a wide range of cell types in the mandible and maxilla, including bone-forming osteoblasts, cartilage-forming chondroblasts, odontoblasts that produce dentin, pulp cells, and tendon and ligament precursors [13, 14]. Therefore, the mechanism that controls diverse cell fates in the cranial neural crest has long been an important area of research. We will highlight several recent studies that used single-cell transcriptomics to explore the complexity of this population.

As the first pharyngeal arch develops, the oral ectoderm is initially patterned into several subdomains. In mice, the proximal and distal portions of the oral ectoderm express *Fgf8* and *Bmp4*, respectively, at E9.5, which help specify the molar and incisor fields along the proximal-distal axis of the arch [15–17]. Ectodermal cells at

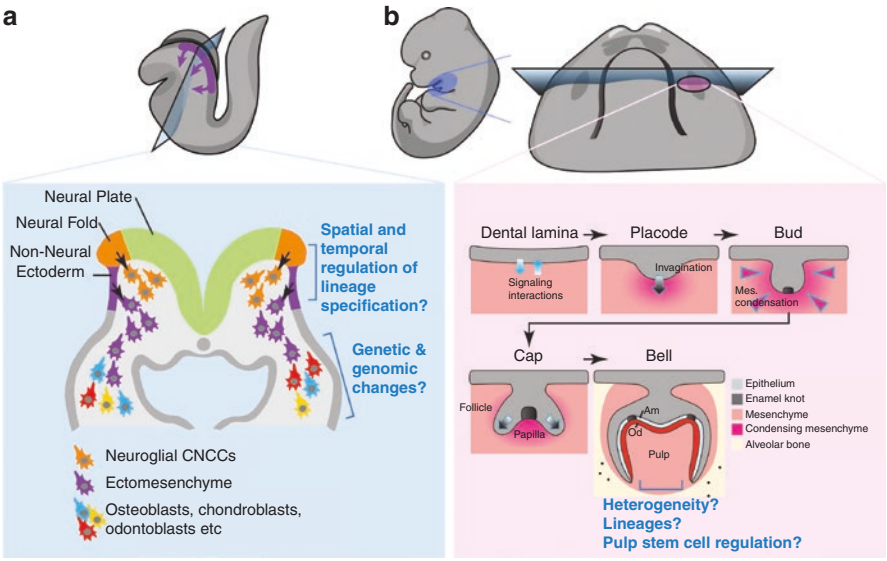

Fig. 19.1 Ectomesenchymal development and tooth formation. (**a**) Ectomesenchyme is formed from the non-neural ectoderm adjacent to the neural fold prior to its closure. Ectomesenchymal cells delaminate from the ectoderm as a result of epithelial-to-mesenchymal transition (EMT) and migrate into the developing pharyngeal arches. They give rise to several cell types, including osteoblasts, chondroblasts, and odontoblasts. However, the spatiotemporal dynamics of specification has been a long-standing question, as are the associated genetic changes. (**b**) Signaling interactions between the forming dental epithelium and the underlying ectomesenchyme drive tooth development and morphogenesis. Mesenchymal condensation takes place during early differentiation of the dental mesenchyme, which proceeds to form the dental follicle and papilla. Papilla then develops into the heterogeneous tissue of the dental pulp. Little is known about the different pulp cell populations, how they are formed, and how they are regulated. *Am* ameloblasts, *Od* odontoblasts

the tooth field then become thickened and begin to stratify, forming the dental placode that bends toward the underlying ectomesenchyme [18]. Subsequent tooth development depends on a series of reciprocal signaling interactions between epithelium and mesenchyme. Signals from the epithelium specify the ectomesenchyme toward the dental mesenchymal fate, while the mesenchyme induces further development of the dental placode. As epithelial-mesenchymal interactions also underlie the development of other ectodermal appendages, such as salivary glands, taste buds, and hair, comparing the signaling responses between these organs will shed light on mechanisms that drive the development of ectodermal organs and how they generate diverse cell types and distinct morphologies.

In response to the signaling interactions, the tooth placode further invaginates into the dental mesenchyme and undergoes a series of morphological changes from a bud, through a cap, and then to a bell-shaped structure (Fig. 19.1b). Concurrently, the dental mesenchyme condenses around the developing tooth epithelium. Mesenchymal cells within the epithelial cap, now called the dental papilla, give rise to dentin-forming odontoblasts and dental pulp, while the

mesenchyme encapsulating the dental cap and papilla, also called the dental follicle, differentiates into various tissues, including the periodontal ligament, the cementum, and the alveolar bone [19]. The dental mesenchyme is thus capable of forming multiple cell types. Nevertheless, key questions relating to the extent of cellular heterogeneity in the dental pulp, when different cell lineages arise, and how the specification of each cell type is regulated (Fig. 19.1) remained largely unresolved, until recently developed single-cell technologies provided the means to address them.

In erupted teeth, the tooth pulp continues to maintain a group of dental pulp stem cells, which help repair injured dentin by forming new odontoblasts in a process known as reparative dentinogenesis [20]. Remarkably, these stem cells are also capable of differentiating toward a wide range of other lineages under different in vitro or in vivo conditions, acquiring odontogenic, osteogenic, chondrogenic, myogenic, adipogenic, or even neurogenic fates [21]. In this context, single-cell technology again offered scientists a powerful tool to dissect the dental pulp populations in mature teeth and to explore potential mechanisms that regulate this regeneration process. We discuss these studies in more details later, following a brief overview of the scRNA-seq technique.

19.1.3 Basic Principles of scRNA-Seq

The goal of this section is to provide a synopsis of the scRNA-seq methodology. For a detailed explanation of the underlying technology, experimental and computational procedures, the reader may refer to other resources [22–25]. Notably, scRNA-seq encompasses a range of platforms that use different methods to isolate single cells and different chemical methods to generate the sequencing libraries [26]. The commercially available, microfluidics-based 10× chromium system is widely used by biologists, including many papers we discuss herein. In addition, single-cell technology is not limited to measuring gene expression levels, as it also includes applications for measuring DNA methylation, chromatin accessibility, protein expression, etc [27]. However, we focus on the more mature technology of RNA-seq, which has been employed in most of the recent pulp studies.

scRNA-seq technology enables profiling the transcriptomes of thousands of individual cells from one or multiple samples. A transcriptome is the whole set of messenger ribonucleic acid (mRNA) molecules that are expressed by a biological sample, whether it is a cell, a tissue, an organ, or an organism. These mRNAs carry information that the cellular machinery uses to build proteins and, thus, each mRNA represents the transcriptional output, or transcript, of a gene. The main advantages of scRNA-seq technology are its ability to quantify transcripts at single-cell resolution, its unbiased nature, and its power to detect rare cell populations that would be missed in bulk sequencing, where the average gene expression from the entire tissue is measured [28]. scRNA-seq does not depend on purification of discrete cell populations, which is often biased by the use of predefined markers. Thus, for studying developing organs, it offers high sensitivity to the heterogeneity of cells and to intermediate transition states during differentiation.

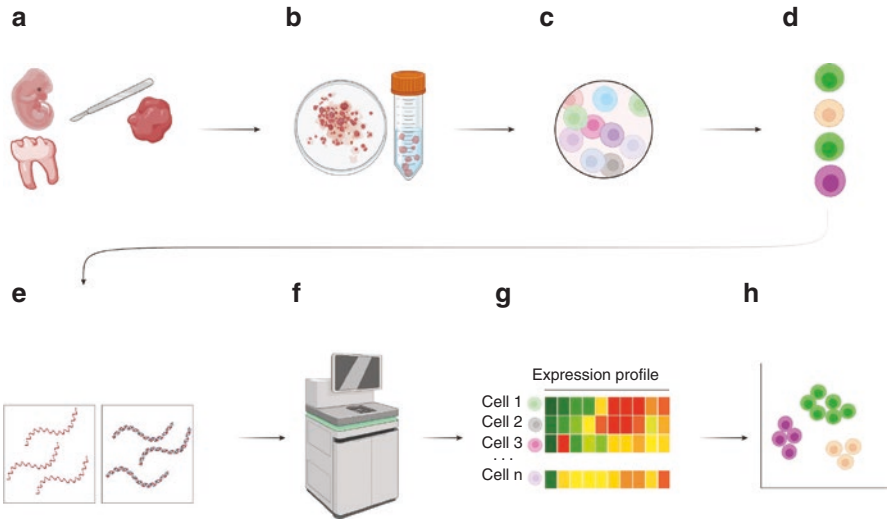

Fig. 19.2 General workflow of scRNA-seq. (**a**). Tissue dissection and cell isolation. (**b**) Single-cell dissociation by enzymatic or mechanical methods. (**c**) Lysing of viable single cells releases their mRNA. (**d**–**g**) Barcoding and library preparation are followed by sequencing and gene expression profiling. (**h**) Bioinformatic tools are used for dimensional reduction and visualization of the data. (*Created with* BioRender.com)

Acquiring a sufficiently high number of healthy cells is a critical first step in conducting a successful scRNA-seq experiment. Therefore, it is essential to empirically determine the appropriate cell dissociation methods and conditions for the tissue of interest prior to the actual experiment [29, 30]. The subsequent steps of scRNA-Seq (Fig. 19.2) are isolation of dissociated single cells (e.g., using microfluidics or fluorescence-activated cell sorting (FACS)), lysing viable single cells to release their mRNA, generation of cDNA such that cells are individually tagged and barcoded, and construction of high-throughput, next-generation sequencing

libraries. The result is a set of sequencing reads that are specific to individual cells, which are then matched to the reference genome or transcriptome to retrieve their identities. Numbers of reads for each gene are converted into expression estimates, which are corrected through normalization and scaling across all cells. Such normalized expression estimates are then used as the input for dimensional reduction and visualization platforms, which group similar cells together, annotate them, and identify differentially expressed genes between groups. A large array of downstream bioinformatic tools have also been developed to enable the prediction of many additional variables, such as cell trajectories, cell-cell interactions, transcription factor enrichment, and function enrichment.

While the basic steps of scRNA-seq are translatable between studies, certain limitations and challenges should be considered when designing scRNA-seq experiments to study tooth development and pulp biology, as well as when interpreting their results. For example, delicate and fast dissection is required to isolate the target cells, which are encapsuled within a mineralized shell. Relative to other organs, the yield of viable cells from each tooth is low and enzymatic digestion conditions should be optimized to ensure cell viability and separation [31]. The relatively small number of sequenced cells also demands rigorous downstream analyses to ensure correct clustering of cells. One solution to the low cell numbers is to pool cells from several donors; however, this could complicate the validation of the results. As human specimens are scarce, very few samples, sometimes only one tooth per experimental condition, were sequenced in some of the studies presented here. Consequently, additional studies are required to account for biological variability and provide reproducibility.

19.1.3.1 A Methodological Comparison of the Reviewed Studies

While all the studies discussed in this chapter applied well-established scRNA-seq protocols, they differed in several important aspects, as illustrated in Table 19.1. These differences should be considered when interpreting results and comparing findings between studies.

Table 19.1 Summary of the main findings of the studies discussed in this chapter as well as their similarities and differences in study designs, sample preparation, scRNA-seq strategies, and bioinformatic tools

		Study design					Sequencing details					
	Paper	Species	Age/ developmental stage	Tooth/anatomic region	Sample numbers	Health status	Cell isolation	# Cells	# Reads/cell	Sequencing platform	Analyzing platform	Main findings
Formation and patterning of the ectomesenchyme	Soldatov et al. (2019)	Mouse	E8.5–E10.5	Cranial neural crest cells (Wnt1-CreER) isolated from embryo heads	>3 embryos/ sample	NA	FACS	At E8.5, 1345; E9.5, 1088; other regions and timepoints, 300–1400	20,000–35,000	Smart-seq2	PAGODA	Sequential bifurcating fate decisions in NCCs and CNCCs are biased toward the mesenchymal fate during delamination
	Tatarakis et al. (2021)	Zebrafish	12; 14; 18; 20; 24 and 30 h post-fertilization (from the onset to completion of neural crest migration)	Cranial NC cells that contribute to the first pharyngeal arch (PA1) isolated using tg sox10:nEOS after photo-conversion	6–8 embryos/ sample, 1 sample/ timepoint	NA	FACS	Not reported	Not reported	10X Genomics	Seurat	CNCC fate decisions are determined during mid-migration, first through a transitional state and then through bifurcation
	Fabian et al. (2022)	Zebrafish	Embryonic (1.5 and 2 days post-fertilization (dpf)), larval (3 and 5 dpf), juvenile (14 and 60 dpf), and adult (150–210 dpf) stages	Cranial neural crest-derived cell isolated using tg sox10cre	Multiple embryos/ sample; 2 or 3 samples/ timepoint	NA	FACS	scRNA-seq, 58,075; snATAC-seq, 88,177	scRNA-seq, 1,000,000; snATAC-seq, 75,000/ nucleus	10X Genomics	Seurat and Signac	Migrating CNCCs undergo progressive and region-specific chromatin organization changes to acquire specific fates
	Williams et al. (2019)	Chicken	6–7 ss (somite-stage)	Citrine+ NC and surrounding citrine− non-NC cells isolated after electroporation of the cranial NC-specific enhancer NC1	Multiple embryos per sample	NA	FACS	scRNA-seq, 2359; snATAC-seq, 1259	scRNA-seq, 152,318; snATAC-seq, 5923/nucleus	10X Genomics (both scRNA-seq and snATAC-seq)	Seurat	In chicks, fate biases occur before migration and correspond to changes in chromatin accessibility

	Xu et al. (2019)	Mouse	E10.5	Dissection of mandibles	5 mandibles/ sample; 1 sample sequenced	NA	Dissection	10,586	28,339	10X Genomics	Seurat	Complementary Shh and Bmp4 signaling pathways pattern the mandibular arch along the oral-aboral axis
	Yuan et al. (2020)	Mouse	E10.5, E12.5, E14.5	Dissection of mandibles	2 embryos/ sample; 1 sample/ timepoint	NA	Dissection	E10.5, 3058; E12.5, 4705; E14.5, 6788	80,000	10X Genomics	Seurat	In the mandibular arch, mesenchymal cell lineages arise through a stepwise bifurcation process
Tooth development	Wang et al. (2022)	Mouse	E10.5, E11.5, E12.5, E13.5, E14.5, E16.5	E10 and E11, incisor and molars together; E12, E14, molars and incisor separately; E16, also M1 and M2	Multiple embryos/ sample; 1 sample/ timepoint	NA	Dissection	4676–11,025 (depending on stage and tooth)	52,196	10X Genomics	R, Python, Seurat, SCANPY	Identified Cd24a++/Plac8+ coronal papilla cells as a group of odontogenetic mesenchymal cells
	Jing et al. (2022)	Mouse	E13.5, E14.5, E16.5, P3.5, P7.5	Dissection of teeth and surrounding tissues	2 embryos/ sample; 1 sample/ timepoint	NA	Dissection	E13.5, 21,416; E14.5, 26,461; E16.5, 29,766; P3.5, 19,134; P7.5, 15,462	Mean 80,000	10X Genomics	Seurat	Apical papilla cells are bipotent progenitors that give rise to the pulp cells and odontoblasts
	Ye et al. (2022)	Mouse	E9.5, E12.5	Epithelial tissue from the mandible	6 embryos/ sample; 1 sample/ timepoint	NA	E9.5, Dissection; E12.5, FACS	E9.5, 13,081; E12.5, 11,131	E9.5:43,421; E12.5:19,585	10X Genomics	Seurat	The dental epithelium is specified through a progressive regionalization process

(continued)

Table 19.1 (continued)

		Study design					Sequencing details					
	Paper	Species	Age/ developmental stage	Tooth/anatomic region	Sample numbers	Health status	Cell isolation	# Cells	# Reads/cell	Sequencing platform	Analyzing platform	Main findings
Post-eruption and adult stages	Pagella et al. (2021)	Human	18–35 years	3rd molar	5 teeth/1 sample	Healthy	Dissection	Dental pulp, 32,378	50,000	10X Genomics	Seurat	Dental pulp MSCs contain three subpopulations; pulp and periodontium progenitor cells are quite similar
	Shi et al. (2021)	Human	Two different developmental stages (A and D)	3rd molar	2 teeth/1 sample	Healthy	Dissection	9855	28,000	NovelBio Bio-Pharm Technology Co., Ltd	Seurat	Provided a cell interactome landscape for the postnatal pulp and discovered signaling pathways regulating the development of various dental cells
	Opasawatcha et al. (2022)	Human	21–36 years	3rd molar (1-#18, 3-#28)	4 teeth/1 sample	1 healthy, 3 caries (deep and superficial)	Dissection	6810	50,000	Hiseq system (Illumina, USA)	Seurat	Inflammation, resolution, and regeneration may occur simultaneously in deep caries; hematopoietic stem cells could be a source of pro-inflammatory cytokines
	Krivanek et al. (2021)	Human	18–31 years	7 third molars, 6 apical papillae of 3 donors	7 adult teeth; 6 growing teeth	Healthy and caries	Dissection	41,673	NA	Smart-seq2 or 10X Genomics	PAGODA	Growing and even fully developed human pulp contain cell populations with regenerative transcriptomes
		Mouse	2–4 months	Lower jaw incisors, first molars	78 incisors; 48 first molars	Healthy	Dissection	9164	NA	10X Genomics	PAGODA	Found a Foxd1+ multipotent population of mouse MSCs and classified the odontoblast and pulp cell transcriptional states across their differentiation

19.2 Formation and Patterning of the Ectomesenchyme

All tooth-related mesenchymal cells, including odontoblasts, pulp cells, periodontal cells, and associated bones, are descendants of cranial neural crest-derived ectomesenchyme. Understanding the process by which neural crest cells give rise to such diverse populations has therefore been an important quest in developmental biology. One of the key questions is whether premigratory cranial neural crest cells are multipotent, i.e., have the ability to become different cell types, or prepatterned early on to adopt a particular fate (Fig. 19.3). Cell labelling and lineage tracing studies in various model organisms have produced contradictory results, in part because of limitations to precisely label all neural crest cells [32–34]. Several recent studies revisited this decades-old question using single-cell data to computationally determine the timeline of cell differentiation and lineage divergence, which were then verified by in situ hybridization and labelling experiments.

Soldatov et al. [35] used *Wnt1*^{Cre} to label both trunk and cranial neural crest populations in E8.5–E10.5 mouse embryos and then sorted labelled cells for downstream high-coverage sequencing using Smart-seq2. Their results showed that premigratory crest cells are not biased toward any specific fate. However, upon delamination, neural crest at the cranial level begins to exhibit a mesenchymal bias, while the trunk neural crest adopts a neuronal fate (Fig. 19.3). As scRNA-seq analysis allows comparing transcript levels between grouped cell populations, differentially expressed genes can be identified. In addition to marking the population, this conveys information about the regulation and function of the cells. In this manner,

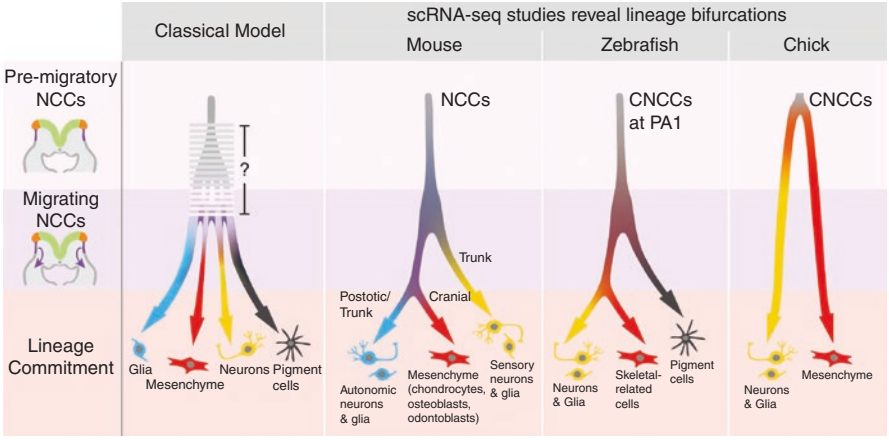

Fig. 19.3 Cranial neural crest cell differentiation in different species. Addressing an enduring question in developmental biology, scRNA-seq analyses revealed that cranial neural crest cells (CNCCs) are specified through different processes in different species. Whereas in mice and zebrafish, specification takes place in migrating CNCCs, in chicks it is already underway in premigratory CNCCs. In addition, while the traditional model posited a single progenitor type giving rise to all differentiated cell types, scRNA-seq studies showed that CNCC differentiation is in fact a series of bifurcation events

the transcription factor TWIST1 was found to be specifically expressed in the delaminating cranial neural crest. Functional studies showed that it drives the specification of a mesenchymal fate [35]. Fate determination thus takes place during migration of neural crest cells and follows a series of binary bifurcation points, where the initially coactivated transcriptional programs of competing cell fates give way to one fate-specific and committed program (Fig. 19.3). Such a stepwise binary process is also observed in the migrating cranial neural crest cells of zebrafish. By combining scRNA-seq data from multiple developmental stages in zebrafish with pseudotime analysis, which infers temporal lineage progression, transitional cells with dual fate markers were detected at bifurcation points [36]. Specifically, migrating neural crest cells first adopted a transitional state, expressing both pigment and skeletal cell markers, and then split into two distinct cell types. In the next bifurcation point, skeletal precursors gave rise to neural/glial cell populations (Fig. 19.3). The order and pattern of neural crest differentiation in zebrafish are thus distinct from those observed in mice.

A second zebrafish study integrated scRNA-seq with single-nucleus assay for transposase accessible chromatin sequencing (snATAC-seq), which interrogates chromatin accessibility. This study revealed that progressive chromatin remodeling underlies transcriptional changes and differentiation of migrating cranial neural crest cells [37]. In chick embryos, changes in chromatin accessibility also explain early fate decisions between neural and canonical/mesenchymal programs [38]. Surprisingly, unlike in mice and zebrafish, cell fate segregation occurred in chick premigratory cells (Fig. 19.3). The discrepancies between these studies may reflect differences among species, as well as between cells from different stages and locations. It should also be noted that while zebrafish do not form oral teeth, they develop pharyngeal teeth from mesenchymal cells of the seventh arch. These cells begin to express tooth transcriptional signatures by 3 days post-fertilization, following placode formation from the endodermal epithelium [37, 39]. On the contrary, mammalian dental mesenchyme is derived from the first pharyngeal arch and induced by signals from the oral ectoderm. As only early migrating cranial neural crest cells were examined in the mouse study described here, tooth-specific transcriptional signatures were absent.

As ectomesenchymal cells populate the developing first pharyngeal arch, they are patterned along different axes. For instance, as mentioned above, Fgf8 and Bmp4 pattern the proximal-distal axis of the mandibular arch ectomesenchyme by respectively activating the expression of transcription factors *Barx1* in the proximal arch and *Msx1/2* in the distal arch [40]. However, the mechanism that determines oral-aboral patterning remained elusive until recently, when a scRNA-seq analysis of E10.5 mouse mandibular arch revealed complementary hedgehog and BMP signaling events in the oral and aboral parts of the mandible [41]. Sequencing results informed subsequent functional studies, which employed both genetic ablation and ectopic activation of hedgehog signaling in postmigratory neural crest cells. These experiments demonstrated that hedgehog acts by inducing the expression of transcription factors *Foxf1* and *Foxf2* in the oral ectomesenchyme, which in turn delineate BMP signaling in the aboral region, thus patterning the mandibular

arch along the oral-aboral axis. By integrating scRNA-seq results from E10.5–E14.5 mandibular arches, a second study showed that mesenchymal cells from the proximal arch either migrate to, or give rise to, cells in the more distal arch [42]. Concurrently, these cells undergo fate determination through a stepwise bifurcation process, splitting first into a stromal cell lineage and a common progenitor population, and then to separate odontogenic/osteogenic and chondrogenic/fibroblast lineages. This sequential lineage restriction manner produces the earliest odontogenic populations.

19.3 Odontogenesis from Bud to Bell Stages

Odontogenesis, which encompasses tooth development through bud, cap, and bell stages, is a well-coordinated process. Decades of research have revealed the complex signaling and genetic interactions between the developing dental epithelium and mesenchyme. However, many outstanding questions remain; for instance, how different cell lineages arise and how their specifications and functions are regulated transcriptionally (Fig. 19.1b). Because tooth morphogenesis in mice is comparable to that in humans, the mouse tooth has served as the primary model system for studying odontogenesis [43]. It should be noted, however, that mice are monophyodont, forming only one set of teeth, and only have incisors and molars, separated by a toothless space called the diastema. In contrast, humans are diphyodont, display sequential development of deciduous and permanent teeth, and form both canines and premolars. Nonetheless, the expression and functions of key developmental genes in teeth are largely conserved across different experimental models [44, 45]. Knowledge gained from recent single-cell transcriptomic explorations of developing mouse teeth [46–48] should therefore be applicable to humans, especially regarding the specification of dental field and cell fate decisions of dental mesenchyme.

Odontogenesis begins in the oral ectoderm with the establishment of the dental placode at around E11 in mice, which is transcriptionally distinct from the rest of the oral epithelium and expresses dental markers such as *Pitx2*, *Irx1*, and *Shh*. It is therefore of interest to understand how the dental epithelium is specified and patterned as a stripe in the dental field. By combining scRNA-seq and spatial mapping of identified genes in the mandibular arch epithelium at E9.5 to E12.5, it was demonstrated that the mandibular ectoderm is initially more homogeneous and broadly expresses tooth-specific transcription factors. These dental-like precursor cells then give rise to both the anterior and posterior non-dental epithelia, which progressively expand and delineate the boundaries of the dental field [48]. The dental field therefore arises as the ectoderm becomes increasingly regionalized at the transcriptional level and the tooth placode is defined by PITX2- and IRX1-targeted gene regulatory networks. Notably, suprabasal cells in the forming tooth bud express many regulators of actin organization and cell motility, enabling epithelial cell rearrangement, which was shown to mechanically power tooth invagination [49].

Although the epithelial signals Bmp4 and Fgf8 have been proposed to specify the incisor and molar tooth types [16, 40], results from genetic perturbation studies

did not yield a definitive evidence of tooth transformation, for example, of molars into incisors [50–52]. The question of how tooth types are specified hence remain open. A recent unbiased investigation of incisor and molar development, where scRNA-seq data from E10.5–E16.5 dental epithelium and mesenchyme were integrated, revealed that although they were identifiable by the respective expression of *Bmp4* and *Fgf8* in epithelium and *Msx1* and *Barx1* in mesenchyme, incisor and molar cells initially had similar transcriptional profiles [46]. However, from E12.5 onward, the incisor and molar mesenchymal cells begin to express unique markers, in part due to changes in chromatin accessibility. Furthermore, computational inference of gene regulatory networks identified *Hand1*, *Alx1/3*, and *Pax3* as potential key transcription factors in the incisor and *Tbx15*, *Lhx6*, and *Tfap2b* as the molar counterparts. Concurrently, transcriptional differences also separate the diastema from the neighboring odontogenic regions [48, 53]. Future works will examine the functional requirement as well as sufficiency of these genes in determining tooth types and diastema fate, providing insight into the genetic regulation of cell populations in the dental field.

Another scRNA-seq study found that as tooth development proceeds, genes important for each stage are upregulated in specific cell populations. Many of these genes are components of signaling pathways, including Fgf, Wnt, Tgfβ, hedgehog, Notch, and ectodysplasin (Eda), reflecting the complex signaling interactions between cells during tooth development [45]. While these signals are essential for tooth morphogenesis and for further development of the dental mesenchyme, how dental mesenchyme gradually gives rise to diverse cell types in the tooth pulp and periodontal tissues is largely unknown. To begin tackling this question, Jing et al. performed scRNA-seq using cells from the mouse molar and surrounding tissues at various developmental time points between E13.5 and postnatal day (P) 7.5 [47]. At E13.5, the *Tfap2b+/Lhx6+* postmigratory ectomesenchyme, which has just committed to the dental fate, appears as a homogeneous population with the potential of giving rise to all dental mesenchymal lineages (Fig. 19.4). At E14.5, the mesenchymal lineage bifurcated into two distinct populations; *Crym+/Egr3+/Fgf3+* dental papilla in the future pulp region and *Epha3+/Fxyd7+/Foxf1+* dental follicle that encapsulates the tooth germ. These fate decisions may be determined by the two highly active gene regulatory networks detected at this stage, one governed by *Barx1* and the other by *Foxf1*, which were enriched, respectively, in the emerging dental papilla and dental follicle [46].

By E16.5, these cells became more diversified, as the dental papilla split into coronal (toward the future crown) and apical (adjacent to the future root) regions, and the dental follicle divided into lateral and apical domains [47] (Fig. 19.4). At P3.5, *Phex+/Ifitm5+* odontoblasts were observed underneath the newly secreted dentin, while the dental papilla consisted of the coronal, middle, and apical populations. Importantly, RNA velocity and pseudotime analyses predicted that apical papilla contains bipotent progenitors that give rise to pulp and odontoblast lineages (Fig. 19.4). Likewise, apical pulp cells were the most proliferative at this stage and

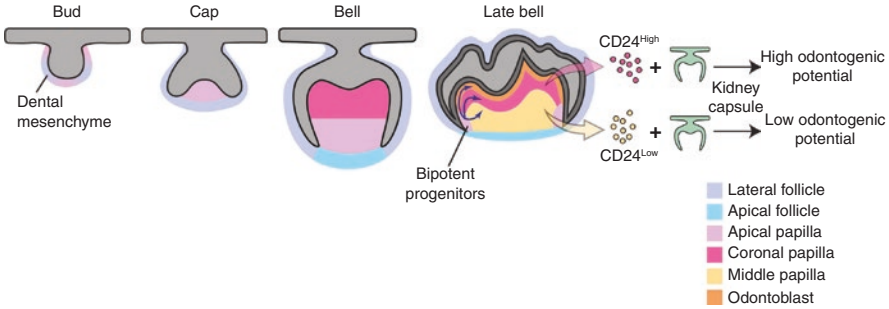

Fig. 19.4 scRNA-seq reveals differentiation of the dental mesenchyme along different cell lineages. Dental mesenchymal cells first give rise to follicle and papilla progenitor cells, which then differentiate into various populations that occupy distinct anatomical positions. At the late bell stage, cells in the apical papilla function as bipotent progenitors that can differentiate into either papilla cells or odontoblasts. Cells in the coronal papilla are characterized by high CD24 expression and retain high odontogenic potential when recombined with dental epithelium and cultured in kidney capsules. Cells with low CD24 expression are comparatively less odontogenic. Together, these findings demonstrate the heterogeneous nature of the dental pulp

their capability to generate both cell types was confirmed by genetic lineage tracing using *Fgf3-CreER*^{T2} to specifically label this population. Differentiation of the dental mesenchyme is therefore a series of bifurcations or trifurcations that generate increasingly diverse and regionalized cell types. Interestingly, several FOX (forkhead box) transcription factors were highly enriched in odontoblasts and different papilla populations at P3.5, such as *Foxj3* in odontoblasts, *Foxn3* in the coronal papilla, and *Foxp4* in the apical papilla. While *Foxp4* is required for proper differentiation of the periodontal ligament [47], it will be interesting to dissect the individual and combinatorial functions of FOX family members in the developing tooth mesenchyme.

The notion that the coronal papilla is a separate mesenchymal population was also demonstrated by Wang et al. (2022), who identified a group of *Cd24a++/Plac8+* cells. Using tissue recombination methods, where sorted or dissected *Cd24a++/Plac8+* cells were recombined, or packaged, with non-odontogenic epithelium and then grown under kidney capsules, they showed that these cells are odontogenic and capable of inducing formation of new teeth. Conversely, *Cd24a+* cells from the apical/middle papilla and *Cd24a-* mesenchymal cells were significantly less odontogenic. These findings imply that whereas cells in the apical pulp function as bipotent progenitors that can form different mesenchymal lineages, coronal papilla cells are odontogenic and can induce the developmental programs of tooth formation (Fig. 19.4). These functional differences should be considered when using pulp cells for regenerative purposes, either to produce an array of mesenchymal cell types or to induce de novo tooth development.

19.4 Post-Eruption and Adult Stages

Tooth growth during the post-eruption phase involves highly coordinated processes, such as alveolar bone resorption, root anchoring, and tissue mineralization. These processes profoundly influence the internal architecture and composition, size and shape of the tooth, and, thereby, its function. Understanding the detailed cellular hierarchies, interactions, and cell type-specific signaling activities during tooth growth is therefore necessary for advancing regenerative approaches. Here too, scRNA-seq offers a unique opportunity to elucidate this process in an unbiased manner and at high cellular resolution.

Based on their transcriptomic signatures, scRNA-seq analyses of growing third molars harvested from human patients revealed all the known cell types of the pulp, including odontoblasts, MSCs, and endothelial and immune cells. These studies also revealed a multitude of novel genes that help classify each cell type within the growing pulp. In many cases, these new markers separated cell types into subpopulations, which could help elucidate cell type-specific functions in the growing pulp. For example, based on differentially expressed markers, both Krivanek et al. [54] and Pagella et al. [55] identified three main types of endothelial cells in the molar pulp. However, the lists of markers slightly differed, likely due to differences in study designs and bioinformatic tools used (see Table 19.1).

Like most biological processes, tooth growth is orchestrated by interactions between cells and transcription factors, often through ligand-receptor complexes. These communication networks could be inferred from the transcriptomic data [56]. For example, by measuring the expression levels of ligands and receptors within each pulp cell type, Shi et al. [57] showed that ligands released from monocytes (IL1B and IL1A), osteoblasts (BMP4, TGFB3, BMP5), and T cells (TGFB1) could function as regulators of renewal genes in apical papilla stem cells. Their computational analysis further predicted that these ligands mainly act on FGFR1, which regulates 28 downstream renewal genes, including *Msx1*, *Ptch1*, and *Sox9*. SCENIC, a computational pipeline that infers gene regulatory networks, predicted *Msx1* as the key transcription factor.

A competent immune system is essential for the dental pulp to oppose microbial infections inflicted by physical injuries to the tooth, gum, or other oral surfaces [58]. Recent scRNA-seq analyses uncovered the detailed composition and organization of the immunocompetent cells within the growing pulp. Analysis of gene expression in different populations enabled inference of their signaling interactions, shedding light on how the immune system operates during tooth growth and development. Interestingly, all analyses of the growing third molars showed that even in healthy teeth, immune cells constitute a larger than expected portion of the pulp cells. This could reflect a heightened state of immune activation during the eruption stage, such as the presence of active macrophages and osteoclasts required to absorb the covering bone. The unexpected high numbers of immune cells may also result from the increased sensitivity of scRNA-seq, as compared to methods such as marker-based flow cytometry. T cells, neutrophils, macrophages, and dendritic cells were identified based on their transcriptomic profiles and, in many cases, further divided into

subpopulations, revealing a previously underappreciated diversity of pulp immune cells. Identifying these distinct cell types also provides clues as to specific immune functions during the pulp growth period. For example, Shi et al. [57] split T cells into eight subtypes and discovered that younger teeth contain more naïve T cells (Th17) and less cytotoxic (CD8T) and memory cells, when compared to a more developed tooth. Krivanek et al. [54] uncovered specific distributions of macrophage subtypes in different pulp domains. Macrophages expressing lymphatic vessel endothelial hyaluronan receptor 1 ($LYVE1^+$) resided away from odontoblast layers, whereas $LYVE^-$ macrophages were scattered ubiquitously and occupied the odontoblast layer as well. It will be interesting to investigate the potential association of these macrophage subsets with specific immune cell homing factors, which could be manipulated to protect teeth against infections.

Transcriptomic comparison between healthy and diseased teeth offers new perspectives on the function of the immune system during injury and subsequent recovery. By comparing the transcriptomes of caries-affected and healthy human molars, Opasawatchai et al. [59] found that immune cell composition in the dental pulp was altered in response to deep, but not superficial, caries, as B cells and dendritic cells were present only in pulp with deep caries. Other scRNA-seq studies also uncovered alterations in the activity level of signaling pathways and predicted certain cell-cell interactions that are likely essential to the pulpal defense mechanisms. For example, based on differences in expression of ligands and receptors between healthy and deep caries teeth, Shi et al. [57] showed that IL1B from monocytes and TGFB1 from T cells regulate dozens of genes that are associated with tooth repair and renewal.

In addition to differentiated pulp cells, recent scRNA-seq-based studies have begun to uncover the diversity and hierarchy of stem cells residing within the dental pulp, known as dental mesenchymal stem cells (DMSCs). Understanding how DMSCs interact with other pulp cells to make cell-fate decisions during growth and repair is key to our ability to use them in a clinical setting. For example, Krivanek et al. [54] found in the apical pulp region of human teeth, where DMSCs reside, two subpopulations of active progenitor-like cells and upstream stromal-like cells. By comparing scRNA-seq data from growing third molars to those of adult non-growing teeth, they found certain apical-distal and growth-related genes in the growing molar alone. Interestingly, an apical-like residual cell population is present also in the adult tooth and could be targeted for reparative responses. Lastly, by assessing gene expression dynamics during the cell cycle in the growing apical papilla region of the third molar, Shi et al. [57] identified genes that may have a role in the apical renewal process.

19.5 Summary

The ultimate goal of dental research today is to find a way to replace injured or missing teeth with newly grown tissues. The dental pulp, which harbors a reservoir of stem cells, holds great promise for realizing that goal. The integration of

single-cell technologies in dental research has considerably enhanced our ability to identify the diverse cell types that populate the tissue, infer their trajectories, and uncover principal genes and pathways that regulate pulp development and function. This technology continues to mature and improve, benefitting from better methods for sample preparation, workflow automation, and intuitive computational tools for robust and informative analyses, as well as from decreasing sequencing costs. Thus, single cell-based approaches are expected to become a basic and powerful tool in both basic and clinical research, as well as in diagnostics and personalized medicine.

Acknowledgments We apologize sincerely to those authors whose work we are unable to cite here owing to space constraints. Many of the scRNA-seq studies discussed here include excellent analyses of cells beyond the dental pulp, which were unfortunately omitted due to the focus on pulp development. The preparation of this book chapter was supported by the BSF grant 2021007 to J.K.H and A.S; NIH/NIDCR grants R03DE030205 and R01DE030471 to J.K.H; and the Israel Science Foundation grant 604/21 to A.S.

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20 Biological Basis for Repair and Regeneration in Modern Endodontics and New Treatment Considerations

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20.1 Introduction

Achieving long-lasting and complete pulp regeneration in teeth with deep caries or severe trauma remains a significant clinical challenge. In teeth with immature apices and exposed vital pulp tissue, partial or complete pulpotomy is typically indicated to preserve pulp function and allow for continued root development. In cases where injury caused pulp necrosis and arrested root development, teeth may remain with poor crown-to-root ratio, a root with very thin dentin walls, and an open apex. The ideal treatment in such cases is to regenerate a functional dentin-pulp complex that would enable completion of root development and thickening of dentinal walls. Emerging evidence suggests that this can be achieved with the recruitment of apical stem cells toward the root canal and/or the transplantation of stem cells using a tissue engineering-based approach. In this chapter, we will discuss the evidence that provides the rationale for stem cell-based regenerative approaches for treatment of pulp injury or pulp necrosis.

Conservative pulp therapies have been used for many years in an attempt to maintain pulp vitality in teeth with injury. However, with the discovery of the function of stem cells in dental pulp tissue [1, 2], the search for biological approaches that exploit these cells for pulp regeneration has intensified exponentially. It is well known that the dental pulp is vulnerable to insults, such as caries, infection, and trauma. While current approaches for treatment of these conditions focus primarily on the maintenance of the compromised tooth structure, future approaches have as ultimate goal the complete regeneration of dental tissues (i.e., dentin and pulp), even in cases of pulp necrosis in young teeth [3, 4]. With the emphasis on tissue regeneration and maintenance of tooth viability, these new concepts of regenerative endodontic procedures aim at enhancing the strength of the tooth and sustain (or recover) pulp vitality [3–5].

With the isolation of postnatal stem cells from various sources in the oral cavity and the development of biocompatible materials for cell and/or growth factor delivery, possibilities for alternative, cell-based treatments are becoming more feasible. Interdisciplinary approaches will be needed to move from replacement to regeneration, involving clinicians as well as cell biologists and material scientists. In this chapter, we will first discuss mechanisms physiology and repair of the pulp-dentin complex, which can be applied to recreate signaling events to inspire dental tissue engineering. Then, we will briefly discuss the biological basis for regenerative endodontics, as well as the potential of the pulp and periapical tissues to regenerate. We will focus on the role of stem cells in repair and regeneration. Finally, we discuss two of the most current pulp regeneration approaches that use stem cells and tissue engineering principles. In projecting future directions, we conclude with a brief discussion of key components necessary to develop effective strategies for dental pulp regeneration, which might enable us to implement novel regenerative strategies in clinical practice in the near future.

20.2 Mechanisms of Pulpal Physiology and Repair

20.2.1 Reaction of Dentin and Pulp to Mild Injury: Healing, Regeneration, and Repair

The ability of odontoblasts to respond to injury (e.g., caries, cavity preparation) and upregulate their secretory activity resulting in deposition of reactionary dentin is well-established [3]. A critical feature of this response is that the odontoblasts have to survive the injury. This is in contrast to reparative dentinogenesis, where the intensity of the injury is of a magnitude that results in odontoblast death and cell replacement by a new generation of odontoblast-like cells [3, 4]. The process of reactionary dentinogenesis involves upregulation of odontoblast activity, often in quiescent cells at the stage of physiological secondary dentinogenesis in response to the injury stimulus. The nature of the signaling process from this stimulus may be rather variable and has been hypothesized to result from the release of growth factors and other bioactive molecules from the dentin matrix during injury [5]. Consequently, the induction of signaling events in these cells are not identical to those observed in primary dentinogenesis and lead to differences in composition and structure of the resulting mineralized tissue. By definition, reactionary dentin is secreted by surviving odontoblasts, and thus other pulp cells are not involved in its synthesis. A variety of bioactive molecules may participate in the signaling of reactionary dentinogenesis, although relatively few have been characterized. Members of the TGF-family, including TGF-1, TGF-3, and BMP-7, are capable of upregulation of matrix secretion [6–8] although there may be other molecules that are capable of participation in these signaling processes.

The relationship between the degree of injury that an odontoblast can withstand and still survive is unclear. Correlation of caries lesion progression and reactionary/reparative dentinogenic events is hampered by lack of chronological information on tissue changes that would distinguish odontoblast survival and renewal [9]. Morphological changes in odontoblasts beneath caries lesions have been reported [10]. In very active lesions, tertiary dentinogenic processes may be absent altogether [11]. However, these data do not allow for discrimination of reactionary from reparative dentinogenesis. Similar problems can exist in the study of pulpal responses beneath cavity preparations where surgical procedures can cause odontoblast cell death [12]. Nevertheless, examination of the relationship among depth of cavity preparation, odontoblast numbers, and the tertiary dentinogenic response beneath the cavity indicates that if the cavity is prepared carefully enough, extensive odontoblast loss is seen only when pulpal exposure is approached [13, 14]. Cooper and colleagues (2011) demonstrated that the depth of the carious lesion is a critical factor, where a full host response is observed in lesions where the remaining dentin layer is less than 0.5 mm. Furthermore, the caries progression rate plays an important role, where rapidly spreading lesions are characterized not only by a different consistency and color but also by a differing microbiota [15]. In slowly progressing lesions, mineral deposition can detain invading bacteria and restrict tissue damage [16]. Pathogen removal by therapeutic intervention can result in the resolution of

inflammation, the elimination of remaining toxins, the secretion of anti-inflammatory signals, and the production of tertiary dentin. However, there is a close link between inflammation and repair, and many proinflammatory mediators in pulpal inflammation can have differential effects [17] depending on their concentration. Compounds, such as TGF-® and TNF-⟨, but also bacterial components can promote processes of repair at low concentrations, whereas they can cause detrimental effects at higher levels. In addition, stem cell differentiation may be controlled by various proinflammatory mediators [18]. Not only the initial inflammatory response but also the reparative phase is characterized by the migration of various immune cells. Furthermore, nerve fiber sprouting beneath the site of injury [19, 20] is guided by pulp fibroblasts by means of complement activation and secretion of brain-derived neurotrophic factor (BDNF), which enhances the outgrowth of neurites [21]. Other neurotrophic factors such as substance P (SP), calcitonin gene-related peptide (CGRP), and neuropeptide Y (NPY) may also play a role during regenerative processes as they promote angiogenesis and stimulate the deposition of tertiary dentin [22, 23]. Both nerve growth factor (NGF) and BDNF are expressed in pulp cells and have been implicated in odontoblast differentiation and thus dentinogenesis [24–26].

20.2.2 The Pulp-Dentin Complex and Conventional Root Canal Treatment

Teeth are complex organs comprising several mineralized matrices, which enclose a soft tissue termed the dental pulp. A healthy dental pulp fulfills a number of different tasks, namely, formation of dentin, perception of pain, and transmission of sensory stimuli from the pulp-dentin complex [27], immunoresponse and cellular clearance of pathogens, as well as formation of dentin as active defense mechanisms against invading toxins and bacteria [28, 29]. In young patients, a functional pulp tissue is essential for the completion of root formation [30]. Irritation caused by caries or trauma induces an inflammatory tissue response termed pulpitis. Initially, this inflammatory reaction may be fully reversible, and healing is possible. However, without therapeutic intervention and with increasing intensity of the stimulus, the inflammation will likely progress to an irreversible state. Traditionally, the therapeutic consequence is to sacrifice the pulp tissue and initiate root canal treatment to prevent further bacterial spreading into the periapical tissues. The procedure includes the removal of vital or necrotic pulp tissue, preparation, enlargement, and disinfection of the root canal system and finally filling with a synthetic material. Root canal treatment offers high success rates, which are influenced negatively by the presence of bacteria in the root canal system and existence of periapical lesions prior to treatment [31]. A common complication that entails retreatment or extraction of the tooth is repopulation of the root canal system with microorganisms due to remaining bacteria in inaccessible areas or due to permeable root fillings or coronal restorations [32]. Additionally, dentin is suspected to undergo mechanical alteration after root canal treatment, which makes root-filled teeth more prone to fracture [33]. Another cause for premature extraction of teeth with root fillings is the

development of caries. The presence of a vital pulp could provide biological defense mechanisms such as maintenance of interstitial pulp pressure [34] and tertiary dentin formation to counteract bacterial invasion, as well as maintenance of nociception to sense damage [27] and enabling timely therapeutic intervention upon progression of caries lesion in close proximity to the pulp tissue.

Regenerative approaches have gained increasing interest in the field of endodontics in recent years. Vital pulp therapy is widely advocated for teeth diagnosed with reversible pulpitis. However, traditional diagnostic schemes are still up for discussion, and preservation of the healthy parts of the pulp rather than complete extirpation is under consideration even for selected teeth diagnosed with irreversible pulpitis [35, 36]. The maintenance of pulp vitality is particularly critical in young patients with incomplete root formation. Bacterial infection and subsequent degeneration of pulpal tissue in children and adolescents is mainly due to traumatic impact. Trauma affects mostly central and lateral maxillary incisors, an aesthetically highly relevant area, with a prevalence of 20–30% in young patients [37]. Immature teeth have large root canals, wide apical foramina, and thin, fracture-prone dentin walls, which make root canal preparation and filling difficult. Cvek (1992) reported on the incidence of cervical root fractures in immature root-filled teeth, which ranges between 28 and 77% depending on the stage of root development and is significantly higher than in mature teeth. The loss of permanent anterior teeth in young patients due to trauma causes major esthetic, functional, and social consequences until dental implants can be considered after growth is complete in adults. Even then, as shown in dental implant studies, facial growth might not be finalized leading to a progressing infraposition of implants over the years and aesthetically unfavorable results [38]. Infection, collapse, and growth arrest of the alveolar bone after premature tooth loss make aesthetically appealing and functional reconstruction a complex and challenging task. These facts emphasize that revitalization or guided endodontic tissue repair has been established as a treatment alternative to traditional root canal therapy or apexification [39]. As such, advantages of pulp regeneration over conventional root canal treatment can be considered as (1) maintenance or restoration of pulp vitality; (2) immune response and interstitial tissue pressure against invading bacteria and toxins; (3) pain perception as a warning system; (4) moist, less fracture-prone dentin; (5) formation of reactionary or reparative dentin to separate the pulp from the site of injury; (6) completion of root formation in young patients to strengthen thin dentin walls and prevent long-term complications; and (7) restoration of healthy periradicular tissues.

20.2.3 Regenerative Potential of the Dental Pulp and Periapical Tissues

The dental pulp is a complex tissue containing odontoblasts, fibroblasts, macrophages, endothelial cells, dendritic cells, lymphocytes, Schwann cells, and progenitor/stem cells [40]. Fibroblasts, macrophages, lymphocytes, and Schwann cells have a limited lifespan and limited capacity for cell division [41]. Odontoblasts are

post-mitotic cells incapable of cell division [40, 42]. Differentiation of primary odontoblasts during embryonic tooth development requires crosstalk between the epithelial cells of the inner enamel epithelium and neural crest-derived ectomesenchymal cells in the dental papilla [40, 42, 43]. During crown dentinogenesis, the ectomesenchymal cells in the dental papilla, which are aligned adjacent to the inner enamel epithelium, receive inductive signaling molecules sequestered in the base membrane from the epithelial cells and differentiate into primary odontoblasts [42, 44–46]. They subsequently produce crown dentin [45]. In teeth with complete crown formation, the inner enamel epithelium disintegrates. Similar to primary odontoblast differentiation in crown dentinogenesis, the primary odontoblast differentiation in root dentinogenesis also requires crosstalk between the inner epithelial cells of Hertwig's epithelial root sheath (HERS) and ectomesenchymal cells of the apical papilla [47]. When primary odontoblasts are destroyed by caries, trauma, mechanical insult, or chemical cytotoxicity, progenitor/stem cells in the dental pulp are capable of differentiating into odontoblasts upon stimulation by appropriate inductive signaling molecules [1, 48]. The periapical tissues consist of cementum, periodontal ligament, and alveolar bone. Fibroblasts, epithelial cells, cementoblasts, osteoblasts, macrophages, endothelial cells, Schwann cells, and progenitor/stem cells are resident cells of the periodontal ligament [40]. Except for progenitor/stem cells, other resident cells in the periodontal ligament have a limited lifespan and a limited capability for cell division. Differentiation of primary cementoblasts requires crosstalk between HERS cells and neural crest-derived ectomesenchymal cells in the dental follicle. The ectomesenchymal cells receive inductive signaling molecules from the epithelial cells of HERS and differentiate into cementoblasts [40, 42, 43]. Therefore, HERS cells play crucial roles in root development and root dentin and cementum formation [49, 50]. In mature teeth, the HERS cells break down into nests of epithelial cell rests of Malassez in the periodontal ligament [40, 50]. When primary cementoblasts are destroyed by trauma or periodontal disease, progenitor/stem cells in the periodontal ligament are capable of differentiating into cementoblasts, adipocytes, and collagen-forming cells upon stimulation by appropriate inductive signaling molecules [51]. Bone marrow-derived mesenchymal stem cells in the alveolar bone are also capable of differentiating into osteoblasts, chondrocytes, and adipocytes upon stimulation by appropriate inductive signaling molecules [52, 53].

20.3 Biological Basis of Regenerative Endodontic Procedures

During tooth development, ectomesenchymal cells differentiate into dentin-forming odontoblasts to produce the dentin matrix and to form the pulp-dentin complex. As root formation progresses, epithelial cells of Hertwig's root sheath (HERS) instruct the underlying mesenchymal cells in the dental papilla to form dentin and pulp tissue of the root [54]. Root formation is completed approximately 3 years after the

crown has entered the oral cavity. The formation of root dentin and pulp happens by differentiation of cells from a specific stem cell niche, the apical papilla. Both the apical papilla and HERS are present only until root formation is complete, and epithelial rests of HERS remain as cells of Malassez and may contribute to repair and maintenance of cementum [55]. A study by Lovelace and colleagues (2011) demonstrated that the provocation of bleeding into the root canal during a regenerative endodontic procedure leads to an enrichment of stem cells from the apical papilla in the root canal, as they are flushed in with the bloodstream. Our understanding is that these cells drive the process of pulpal tissue formation and differentiate to generate new dentin to increase the length and thickness, close an open apex, and complete root formation. The presence of HERS and apical papilla appears to be necessary for true regeneration to take place. Another source of stem cells is the dental pulp itself. Even in teeth with complete root formation, the dental pulp harbors a small percentage of stem cells localized around blood vessels in the perivascular niche [56]. It has been shown that stem cells from inflamed pulp retain their regeneration potential [57]. Likewise, it can be assumed that stem cells of the apical papilla can survive and retain their regeneration potential for prolonged periods of time even in the presence of peri-radicular lesions. Considerations to extend regenerative endodontic procedures to permanent teeth are ongoing [58, 59].

It was recently shown that even in teeth with complete root formation, the provocation of bleeding into the canal results in an influx of mesenchymal stem cells (MSC) [60]. These cells expressed MSC markers, showed a distinct differentiation potential, and were found compartmentalized in perivascular niches in peri-radicular lesions. This interesting finding opens new perspectives and offers a biological basis for such procedures in permanent teeth. However, from a biological and development point of view, it appears more likely to achieve repair rather than regeneration in these cases. Any manipulation inside the root canal, such as the use of irrigants and intracanal medicaments, should be considered under the premise to create the best possible environment for these cells to exert their regenerative potential. In conventional root canal treatment, the contact area with the surrounding tissues is comparably small. The implementation of regenerative procedures requires the practitioners understanding of the biological basis, and how procedural steps of the therapeutic intervention will influence cell survival, migration, angiogenesis, proliferation, and differentiation. This will require sufficient disinfection of the root canal system is as important as to prevent harm to the target cells [61], while at the same time maintaining dentin-derived signaling molecules that are required for pulp tissue regeneration [62]. Thus, pulp regenerative techniques require procedures (e.g., irrigation) that cause minimum damage to cells and dentin-derived morphogenic signals while allowing for efficient disinfection.

20.3.1 Stem Cells in Repair and Regeneration

An important cell source during regular tissue turnover, but also during repair, is the pool of resident stem cells within the dental pulp. Mesenchymal dental pulp stem cells can be harvested from permanent teeth [1], deciduous teeth [2], and the apical papilla of immature teeth with incomplete root formation [47]. Stem cells in the dental pulp located in the perivascular niche [63] remain quiescent until they are recruited to the site of injury upon chemotactic signaling and differentiate into odontoblast-like cells [64]. However, pulp stem cells also express toll-like receptors (TLRs) and are capable of pathogen recognition [65] and may also be recruited after activation by macrophages [66].

Whereas carious lesions are the most common cause for inflammatory reactions, traumatic impact, for example, after crown fractures, may also expose the pulp to the oral cavity and thus enable microorganisms to access the pulp chamber. In the latter case, a healthy pulp can withstand bacterial invasion for several days. Animal studies in monkeys demonstrated that the inflammatory zone did not extend more than 2 mm into the pulp tissue even after 1 week of exposure to the oral cavity [67], which highlights once more the remarkable ability of this tissue to withstand a bacterial attack.

Revitalization or regenerative treatment approaches in teeth with incomplete root formation and pulp necrosis have become part of the therapeutic endodontic spectrum and should be considered as an alternative to conventional apexification. Ideally, regenerative endodontic procedures allow not only for a resolution of pain, inflammation, and periapical lesions, but also for the formation of an immunocompetent tissue inside the root canal which can reconstitute the original biological structure and function of dental pulp and thus lead to an increase in root length and thickness and strength of previously thin, fracture-prone dentin walls. Common features of regenerative procedures performed in immature teeth with pulp necrosis include (1) minimal or no instrumentation of the dentinal walls, (2) disinfection with irrigant solutions, (3) application of an intracanal medicament, (4) provocation of bleeding into the canal and creation of a blood clot, (5) capping with calcium silicate, and (6) coronal seal. Next, we will discuss two strategies that have received much attention recently for revitalization of necrotic young permanent teeth, i.e., stem cell homing and stem cell transplantation for dental pulp tissue engineering (Fig. 20.1).

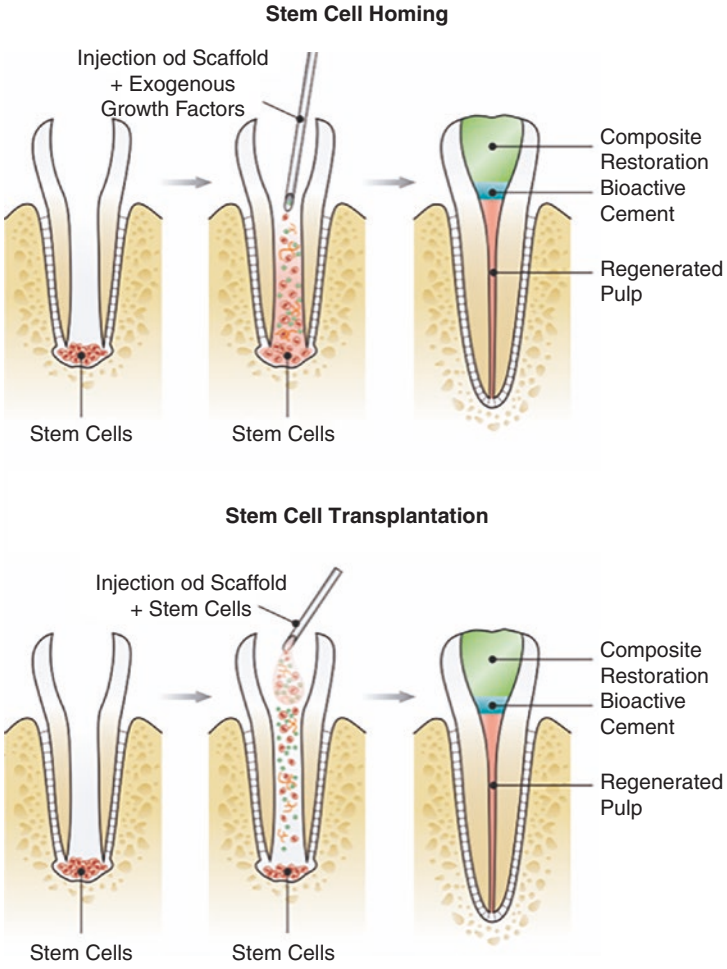

Fig. 20.1 Schematic representation of two strategies for dental pulp tissue engineering. Stem cell homing involves the injection of a cell-friendly scaffold and exogenous growth factors that induce a chemotactic gradient for stem cells from the apical papilla to migrate toward the interior of the pulp chamber and regenerate the dental pulp tissue. Alternatively, stem cells can be mixed in a biodegradable scaffold and injected in the interior of the root canal. In this case, most of the regenerated pulp will be formed by the cells transplanted with more modest participation (if any) of the stem cells from the apical papilla on the regeneration of the dental pulp

20.4 Stem Cell Homing for Dental Pulp Tissue Engineering

Pulp vitality preservation is a major objective in endodontics, as devitalized teeth are more vulnerable and prone to tooth loss later in life [68]. An adequate revascularization is a determining element of success for dental pulp tissue engineering. This is especially relevant when considering that the dental pulp tissue regeneration takes place in a confined space with a sole access for nerve and vasculature supply via the apical foramen. Application of the classic principles of tissue engineering might allow us to better control the involved cells and tissues and lead to more predictable outcomes. Accordingly, the formation of new pulp in empty root canals was shown in animal models by the insertion of scaffolds, cells, and growth factors [69]. This approach is challenged by several obstacles concerning translation and chairside application, namely, the availability of methods for isolation, storage, and expansion of stem cells that follow good manufacturing practice guidelines.

Hence, cell homing (or in situ tissue engineering), i.e., the process in which a primarily cell-free scaffold delivers bioactive cues to recruit resident stem cells and induce their differentiation, has gained increasing attention recently [70]. In situ tissue engineering has been investigated for various possible applications including vascular grafts and nerve and hard tissue regeneration [71]. For in situ tissue engineering (cell homing), the classic tissue engineering triad can be modified to resident stem cells, customized biodegradable scaffold that will promote timely vascularization [72], and endogenous growth factors. Resident cell sources include mesenchymal stem cells from dental pulp [1], apical papilla in immature teeth [47], and the periapical area of teeth with complete root formation [60].

After disinfection, induction of bleeding into the root canal can lead to an influx of stem cells from the apical papilla [73] and new tissue formation. Blood coagulation results in the formation of a three-dimensional fibrin network containing not only blood cells but also cytokines and growth factors that initiate wound healing [57]. Those signaling molecules can promote chemotaxis, proliferation, and differentiation of the stem cells inside the root canal and lead to generation of new tissue. An extension of the respective protocol to mature teeth has been debated [74]. In cases of immature and mature teeth, patients might benefit from less invasive and regenerative-based treatment approaches in which tissue function is restored to exert an immune response and generate a mineralized tissue barrier. Although current clinical protocols show high success rates for this treatment [75, 76], histologic analysis in animal studies [77] and occasional patient cases [78] show that pulp tissue may not regenerate to its original architecture and function but rather repair by the formation of fibrous tissue, cementum, or bone.

A recent study from Widbiller et al. (2018) demonstrated that fibrin-based materials enriched with endogenous, dentin-derived growth factors appear suitable for in situ tissue engineering because they allow for cell ingrowth and pulp like tissue formation. Currently used dental materials can also affect cell homing either indirectly by stimulating the secretion of bioactive molecules by residual pulp cells or directly by their chemical composition. For instance, conditioned medium of DPSCs exposed to mineral trioxide aggregate and growth hormone induced endothelial

tube-like formation and migration [79]. Furthermore, mineral trioxide aggregate was shown to augment angiopoietin 1 and von Willebrand factor expression in DPSCs [80].

Despite the developments of the last few years, dental pulp regeneration via cell homing needs to be further understood and improved. Several aspects need to be clarified to make it achievable and predictable in dental practices [81]. On the whole, the comprehensive knowledge on cell homing for dental pulp regeneration based on the most current literature considers the following:

- The importance of the scaffolds employed; further improvements are in progress, such as nanofibrous technology and antibiotic addition [82].
- The efficacy of growth factors, especially when dentin-derived, as reported in the latest update [69].
- The feasibility and safety of cell homing strategies in mature teeth with vital pulps from animals and subsequently from humans, although better characterization and standardization of the procedures are required [83].

20.5 Stem Cell Transplantation for Dental Pulp Tissue Engineering

When the lost pulp tissue exceeds a critical size, cell homing may not be sufficient to regenerate dentin-pulp tissue, and cell-based treatments may represent a more desirable alternative approach. Considering the relatively ease of isolating dental pulp stem cells (DPSCs) and their multipotential ability, most of the studies use these cells for dental pulp regeneration purposes. Early studies in animal models demonstrated that regeneration of pulp-like tissue was possible after stem cell transplantation in tooth slices, dentin cylinders, and even whole tooth roots using a tissue engineering concept [84–87]. Furthermore, animal models showed new tissue formation in pulpotomies and in pulpectomies after stem cell transplantation [86, 88]. In another study, implantation of DPSCs and platelet-rich fibrin constructs in root fragments in nude mice and in endodontically treated canine root canals led to more pulp-like tissue generation with better vascularization as compared with DPSCs or platelet-rich fibrin alone. This may be attributed to the slow release of growth factors from platelet-rich fibrin acting on the DPSCs [89]. Additionally, a study from Li and colleagues (2016) demonstrated the benefit of combining DPSCs with a VEGF-loaded microsphere-based scaffolding system for full-length human tooth regeneration. The addition of DPSCs was necessary to regenerate blood vessels throughout the entire root canal, which could be explained by DPSC-induced endothelial cell migration and increased growth factor expression. Most recently, a milestone was reached using autologous dental pulp stem cells transplanted into permanent teeth with irreversible pulpitis [90]. In this study, a functional recovery of pulp tissue was shown by detection of a new lateral mineralized tissue by cone-beam computed tomography. In a different study, autologous dental pulp stem cells from deciduous canines were transplanted into permanent immature incisors in

cases of pulp necrosis after dental trauma [91]. In this study, completion of root formation was observed in the treatment group, which was not observed in the control group, where an apical plug was placed.

Animal and human studies provide some proof of principle that pulp tissue regeneration can be achieved by the cell-based approach. However, in clinical practice several challenges have to be overcome, such as availability and isolation of autologous stem cells, storage, expansion, culture, handling, maintenance of sterile conditions, good manufacturing practice facilities, government regulatory policies, and the clinician's knowledge and skill.

20.6 Conclusions

Contemporary dentistry relies heavily on biomaterials to replace lost tissues in the oral cavity. Such strategies restore shape and form but do not necessarily regenerate the physiological architecture and function of the lost tissue. Our understanding of the biology of the pulp has improved significantly in recent years, and this has allowed us to present more robust hypotheses regarding the molecular and cellular processes responsible for dental regeneration. Thus, advances in the field of material sciences, stem cell biology, and dental tissue engineering have raised the possibility of using biology-based treatment strategies developed to regenerate functional dental tissues. Dental pulp stem cells are highly proliferative and have the potential to differentiate into all the different cell types necessary to generate a functional dental pulp. The high proliferation rates, self-renewal, multipotency, and relative ease of access to tissues make the dental pulp an attractive source of mesenchymal stem cells for tissue engineering. Compelling evidence pinpoints that pulp tissue engineering after the transplantation of stem cells is possible. However, severe problems regarding clinical feasibility remain. With that said, cell homing is a potentially suitable alternative that may overcome those challenges. However, the clinicians need to take into consideration that the success of pulp regeneration relies on the clinical and biological conditions of the teeth. Hence, cell homing strategies will not be consistently successful in every condition, such as irreversible pulpitis and pulp necrosis. Root canal treatment remains the standard of care for mature teeth with necrotic pulps and closed apices. Despite such issues, cell homing currently represents a path for dental pulp regeneration because it recruits the patient's own stem/progenitor cells through biological cues to restore the lost and damaged pulp tissue. Stem cell homing and stem cell transplantation for dental pulp tissue engineering might become clinically relevant strategies to enable dental pulp regeneration in the future. However, the broad use of these techniques will require more extensive clinical trials that demonstrate unequivocally their safety and efficacy.

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