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Management of the Vital Pulp and of Immature Teeth

ANIBAL DIOGENES, TATIANA BOTERO, AND MO KANG

CHAPTER OUTLINE

LEARNING OBJECTIVES

After reading this chapter, the student should be able to:

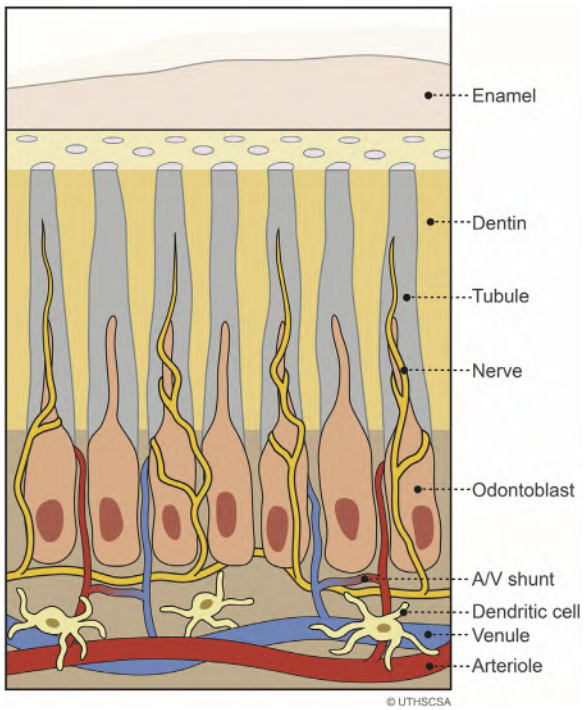
1. Understand the special physiologic and structural characteristics of the dentin-pulp complex and how they affect the pulpal response to injury.
2. Discuss the effects of pulpal injury in teeth with developing roots.
3. Differentiate reparative and reactionary dentin.
4. Recognize the indications, contraindications, and expected outcomes of the vital pulp therapy protocols.
5. Describe diagnosis and case assessment of immature teeth with pulp injury.
6. Determine the techniques for vital pulp therapy and prognosis.
7. Indicate the treatment options for immature teeth with pulp necrosis.
8. Describe apexification procedures and prognosis.
9. Explain the technique and the goals of regenerative endodontic therapy.
10. Recognize the tissue engineering techniques used to regenerating the dentin-pulp complex.
11. Indicate the stem cells present in dental tissues and their potential to regenerate the dentin-pulp complex.

The Dentin-Pulp Complex

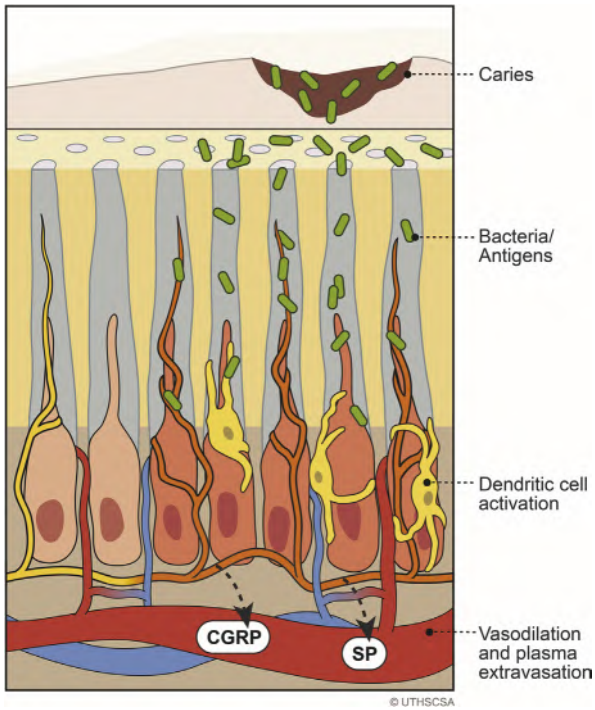
Pulp Defense Mechanisms

The dental pulp is a highly specialized and complex loose connective tissue encased by mineralized tissues, namely enamel, dentin, and cementum. The dental pulp has close anatomic and functional relationship with the dentin, often referred as dentin-pulp complex (Fig. 10.1). Although the dental pulp is protected by a mineralized case, it is not impervious to irritation. Dental caries, trauma, anatomic defects, and iatrogenic mishaps can lead to inflammation and possibly pulp necrosis. However, the dentin-pulp complex has elaborate defense mechanisms.

Invading microorganisms reaching the dentin will encounter an outward flow of dentinal fluid. This positive pressure maintained by the dental pulp acts to "push" out the ingression of microorganisms, and it increases if pulpal inflammation and edema occur. A notable aspect is that this fluid will carry important molecules released from cells of the innate and adaptive immune response such as cytokines, immunoglobulins, and complement proteins.[1] These molecules are able to initiate the pulpal defense before these organisms reach the pulpal cells. In addition, bacteria-mediated demineralization of dentin releases key noncollagenous proteins (NCPs) that mediate reparative responses.[2] Thus dentin is no longer thought to be an inert tissue but instead comprises myriad growth factors, morphogens, and neurotrophins that have shown to be "fossilized" within the dentinal matrix and that can be released upon demineralization and mediate processes of angiogenesis, neurogenesis, and dentinogenesis.[3] These processes are part of an elaborate response of the dentin-pulp complex to increase vascularity, overhauling the immune response and the metabolic demand of an injured area undergoing remodeling, repair, and possibly regeneration.[4] In addition, inflammatory foci within the dental pulp have increased innervation density due to robust neuronal sprouting in the area. These neuronal fibers, mainly nociceptors, play their best recognized role of surveillance by providing nociceptive signals but also participate in the



• **Fig. 10.1** Illustration of the dentin-pulp interphase in normal conditions. The fluid-filled dentinal tubules are occupied by odontoblastic processes and free nerve endings that might extend farther than odontoblasts toward the enamel junction. The subodontoblastic complex is composed of a rich capillary bed and innervation network. The pulp capillaries are equipped with arteriole/venule (A/V) shunts that may open upon injury, diverting the circulation to uninjured areas. Dendritic cells are the main antigen presenting cells in the dental pulp that are usually located in the subodontoblastic process in normal conditions of homeostasis.

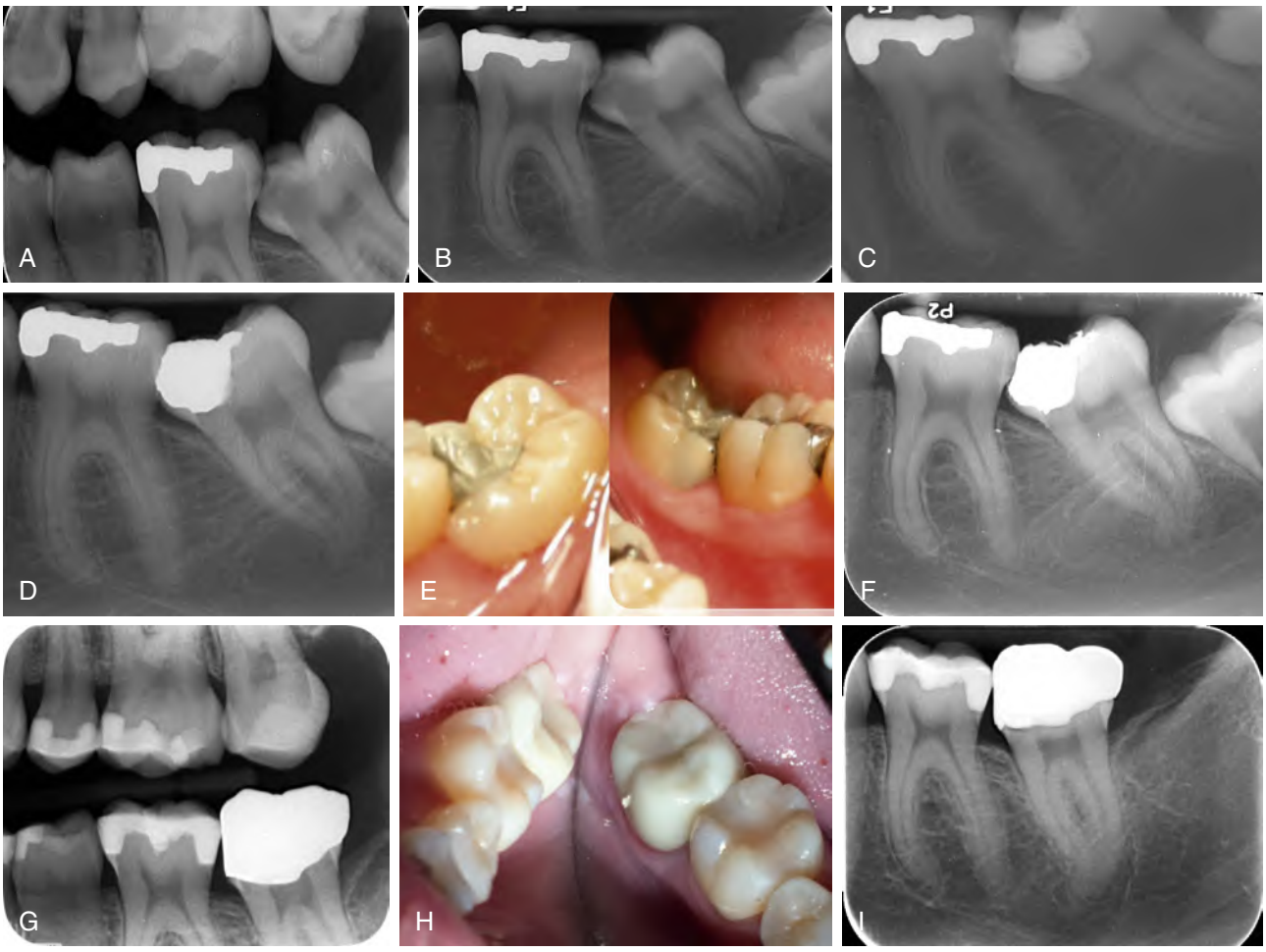


• **Fig. 10.2** Illustration of early events of microbial insult to the dentin-pulp complex. Microbes and their antigens diffuse through dentinal tubules reaching the free nerve endings of the trigeminal ganglia. These neuronal fibers express microbial recognition receptors (i.e., Toll-like receptors) and are activated and sensitized, resulting in the neuronal release of vasoactive peptides (i.e., calcitonin gene–related peptide [CGRP] and substance P [SP]) that, in turn, promote vasodilation and plasma extravasation, also known as neurogenic inflammation. Odontoblasts also express Toll-like receptors that upon recognition of microbial presence, trigger the release of chemokines, attracting dendritic cells to the dentinal tubules. These dendritic cells engulf and digest microbial antigens into epitopes and present these to cells of the adaptive immune cells (i.e., T cells). Subsequent events of pulp inflammation include the exuberant accumulation of polymorphonuclear (PMN) and adaptive immune response cells.

inflammatory process known as *neurogenic inflammation* by the release of vasoactive peptides such as calcitonin gene–related peptide (CGRP) and substance P, which are responsible for promoting vasodilation and plasma extravasation, respectively, as well as modulation of immune cell function (Fig. 10.2).[5]

The progressive ingress of antigen and microorganisms into the dentin first reaches the cells positioned with the dentinal tubules (see Fig. 10.2). These cells include nociceptive primary afferent neuronal terminals that have been shown to extend up to 200 µm into the dentinal tubules and odontoblastic processes (see Figs. 10.1 and 10.2).[6] Interestingly, pulpal neuronal afferent fibers are mainly nociceptors but have also been shown to have a role in directly detecting microorganisms.[7] This characteristic is particularly interesting because the dentin-pulp complex is one of the most densely innervated tissues in the human body with nociceptors. These neuronal fibers within the dental pulp, regardless their degree of myelination, have been shown to mediate only nociceptive signals. Thus teeth are constantly under surveillance of this neuronal network dedicated to detecting injury or potential injury. These neurons have been shown to express the Toll-like receptor 4 (TLR4) that recognizes liposaccharides or endotoxins from gram-negative bacteria.[7,8] The activation of TLR4 in neurons results in sensitization of these fibers, lowering their activation threshold and increasing the response magnitude.[7,8] This increased response, in turn, leads to secretion of vasoactive peptides such as CGRP and substance P (see Fig. 10.2). The action of these peptides results in vasodilation and plasma extravasation (i.e., edema) at the site of injury, a process called *neurogenic inflammation*. The vasodilation and plasma extravasation allow for greater vascularity in the area with increased immune cellular presence and greater outward fluid flow, decelerating the ingress of microorganisms (see Fig. 10.2). This unique neuronal–bacterial communication is a sophisticated mechanism for sensory neurons to detect, alert the breach of the biological barrier, and initiate a process of neurogenic inflammation that will be immediately integrated with the immune-driven inflammation. An interesting aspect is that the early symptoms of a carious lesion can be manifested as painful responses to low-intensity stimuli and exaggerated responses to noxious stimuli in reversible pulpitis, matching the previously described neurophysiology.

Odontoblasts are highly specialized cells that serve the primary role of secreting dentin. As with other cell types within the dentin-pulp complex, these cells also have other functions that extend beyond their best-recognized role as secretory cells. Odontoblasts have also been shown to act as "sentinels" because these cells express many subtypes of TLRs and thus can detect the presence of gram-negative and gram-positive viruses and fungi within the dentinal tubules.[9,10] Activation of these TLRs have been shown to result in upregulation of expression and release of key chemokines and cytokines.[9,11] These factors are crucial for the recruitment of dendritic cells from the subodontoblastic plexus area to the areas



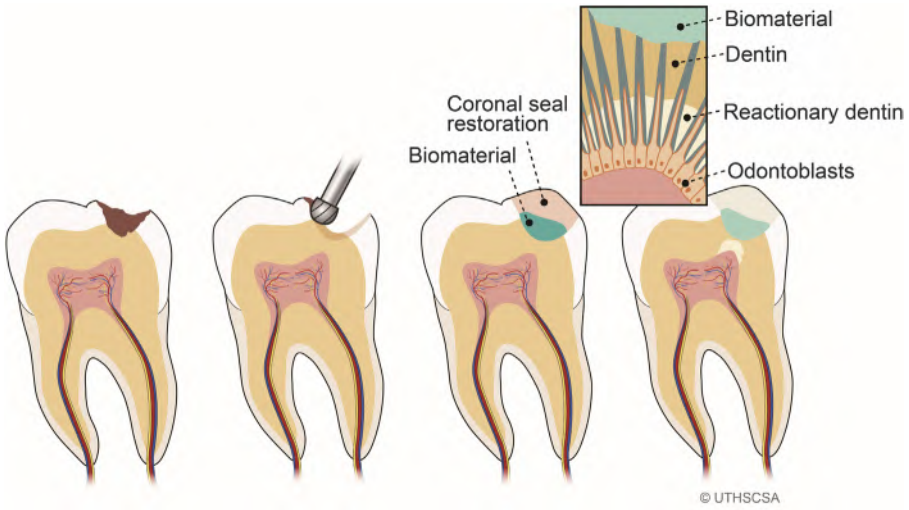
• **Fig. 10.3** Indirect pulp capping. A 14-year-old female patient consulting with symptoms of reversible pulpitis and symptomatic apical periodontitis on tooth #18 (**A** and **B**). Extensive decay and infected dentin were removed, exposed, and sealed with WMTA-ketac silver glass ionomer under rubber dam isolation **(C)**. Final obturation was performed 1 month later with amalgam (**D** and **E**). At 1-year follow-up, the patient was asymptomatic, and tooth #18 responded normal to clinic tests and radiographic evaluation (**F**). At 5.5-year follow-up, tooth #17 had been extracted and tooth #18 had a received a full-cuspal coverage crown. The patient was asymptomatic, and tooth #18 had normal response to clinicals test (**G**, **H**, and **I**). (Courtesy Dr. Tatiana M. Botero, faculty dental practice, University of Michigan, Ann Arbor, MI, USA.)

of insult (see Fig. 10.2). These cells represent the major form of antigen-presenting cells in the dental pulp and are analogous to Langerhans cells in the skin.[12] They are equipped to engulf, process, and present the antigens to other cells of the immune response system. In addition, dendritic cells will release additional chemokines and cytokines that in conjunction with odontoblast-derived factors and neurogenic inflammation will recruit additional cells of the innate and eventually adaptive immune response, resulting in the amplification of the inflammatory process. It is noteworthy that inflammation is a normal homeostatic response and is essential for containing the invasion of microorganisms. If successful, tertiary dentin is deposited in the area of insult in the form of either reactionary or reparative dentin, providing an additional mineralized barrier. Last, the presence of arteriole/venule (A/V) shunts (see Figs. 10.1 and 10.2) that open upon injury[13] allows for the compartmentalization of microabscess regions within the dental pulp that are surrounded by vascularized dental pulp. The careful removal of the infected tissue, allowing the surrounding tissue to promote repair, represents the biologic basis for pulpotomy procedures (Fig. 10.3).

Tertiary Dentinogenesis

The process of dentin mineralization occurs prenatally for most teeth and throughout the life of a tooth as long as the pulp is vital. The primary dentin is formed during tooth development, whereas secondary dentin is deposited at a slower rate, after tooth maturation, resulting in the gradual deposition of dentin throughout the entire extent of the pulp canal spaces and pulp chamber.[14] The most superficial layer of dentin in contact with the dental pulp is the predentin that is formed by the unmineralized matrix secreted by the odontoblasts. It is the mineralization of the predentin that forms the mature primary and secondary dentin that are composed roughly by 70% hydroxyapatite crystals, 20% organic matrix, and 10% water.[15] Thus primary dentin and secondary dentin are deposited in response to normal physiologic conditions. Tertiary dentin, on the other hand, is secreted in response to any injury to the dentin-pulp complex.

A mild injury to the pulp that can provide sufficient inflammatory stimuli for odontoblasts, increasing the secretion of tertiary dentin at a higher rate, promotes "reactionary" dentinogenesis (Fig. 10.4). This reaction of the surviving odontoblasts results



• **Fig. 10.4** Reactionary dentin formation as result of an indirect pulp capping procedure. Upon the removal of infected dentin, the cavity is layered with a biomaterial that stimulates surviving odontoblasts to secrete dentin at a faster rate, creating a localized accumulation of dentin, distancing the pulp from the area of mild injury.

in localized increased thickness of the dentinal layer as it maintains the overall architecture of the dentin odontoblast interphase. Odontoblast death could occur with more intense stimuli for a period of time sufficient to lead to the loss of odontoblasts in the area of injury. If the surrounding pulp remains vital and there is a favorable balance between inflammation and repair, progenitor cells are recruited to the site of injury,[16] possibly by chemotactic factors released from the demineralized dentin matrix and neighboring cells. These progenitor cells differentiate into mineralizing cells often referred as "odontoblast-like cells." Although these cells differ in morphology from native odontoblasts, they also secrete a matrix that upon mineralization forms a "mineralized bridge" over the area of injury called *reparative dentin* (Fig. 10.5). This dentin is typically atubular and, due to its rapid secretion, often traps the mineralizing cells within its matrix resembling osteocytes; it is often referred to as "osteodentin." This nontubular dentin bridge, if formed uniformly without tubular defects, can provide a biological barrier with fluid permeability seen with tubular dentin.[17] This inherent reparative and regenerative capacity of the dental pulp forms the basis for contemporary vital pulp therapies.

Pulp Necrosis and Root Development

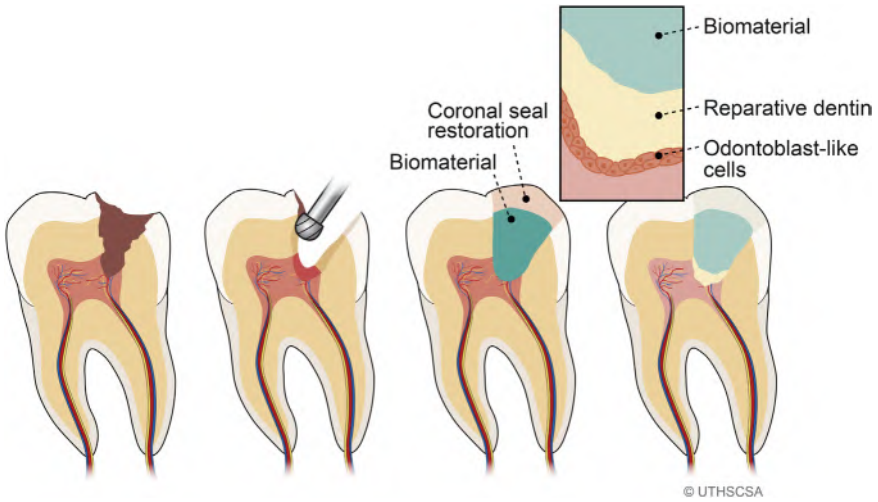
Despite the advanced defense and reparative mechanisms already described in this chapter and in Chapter 1, the dental pulp may succumb to infections. The progressive process of liquefaction pulp necrosis results in complete loss of homeostatic functions. An important factor is that the loss of odontoblasts in the radicular pulp results in arrested tooth development in teeth still undergoing development. Indeed, root development is known to continue 2 to 3 years after the eruption of a permanent tooth in the oral cavity.[18,19] This process of root formation and maturation requires the complex interaction of the epithelial root sheath and mesenchymal cells located in the dental apical papilla.[20] Pulp necrosis and/or trauma can severely disrupt this interaction, resulting in interruption of normal development in addition to the development and maintenance of apical periodontitis. Thus all efforts must be directed toward avoiding complete pulp necrosis through vital pulp therapies. Nonetheless, vital pulp therapy as a treatment alternative depends on the initial clinical presentation and the often-challenging assessment of the degree of inflammation.

Etiologic Factors of the Dentin-Pulp Complex Injury

Preserving the vitality of the dentin-pulp complex tissue is the principal goal when treating teeth that have been damaged by trauma, caries, dental anomalies, or iatrogenic factors. Each of the etiologic factors will cause an initial inflammatory reaction: pulpitis. If not treated, this reaction will progress to irreversible pulpitis, leading finally to necrosis. Recognition of these factors will contribute to the preventive therapeutic approaches and preservation of the pulp vitality. Maintenance of pulp vitality requires a good understanding of the interplay of biologic factors influencing regenerative events such as the infection and the inflammation occurring. Vital pulp therapies may not be suitable for all cases, especially those showing deep pulpal inflammation and involving the periapical tissues. The correlation of clinical symptoms with the pathophysiologic status of the dental pulp remains a significant diagnostic challenge before attempting a regenerative procedure, for example.

Trauma

When patients present with traumatic dental emergencies, management is crucial for the prognosis of the tooth. It is important to perform an extensive evaluation and diagnosis of the case as well as schedule adequate follow-up visits to detect possible complications such as pulp necrosis and resorptions. The incidence of dental trauma is higher among boys than among girls, and the anterior maxillary teeth are the most commonly affected teeth,[21,22] particularly in patients with increased overjet and active participation in sports.[23-27] The incidence of dental trauma has overall (all ages) a frequency of 5%, but in 0- to 6-year-old patients it is 17%.[28] Traumatic injuries are more common in permanent (58%) than in primary teeth (36%).[29,30] The maxillary central incisor is more frequently affected (66%) than is the lateral incisor (17%). Uncomplicated crown fractures (without pulp exposure) are the



• **Fig. 10.5** Reparative dentin formation as result of a direct pulp capping or partial pulpotomy. Upon the removal of infected dentin and part of the injured pulp, the cavity is layered with a biomaterial that stimulates migration of pulp progenitor cells (such as a tricalcium silicate material) and the differentiation into mineralizing cells in the area of injury. These cells secrete a mineralized bridge called reparative dentin in the attempt to create a biologic seal between the injured area and the underlying dental pulp.

most common traumatic lesions (41% to 68%).[23,24,26] Pulpitis and necrosis can also occur as a result of dentinal exposure to bacteria and bacterial byproducts in uncomplicated (nonpulp-exposed) or complicated (pulp-exposed) crown or crown-root fractures. The incidence of pulp necrosis after uncomplicated crown fractures is low (2% to 5%), but when there is a concomitant injury such as a luxation the chances of necrosis increases, especially in cases with a close apex (55% to 65%) compared with open apex teeth (3.5% to 11%). The traumatized dental pulp in immature or open apex teeth will have greater chances to heal and survive.[31-33]

Trauma to the periradicular tissues can disrupt the neurovascular supply of the dental pulp, leading to necrosis. Severe traumatic incidents such as intrusions, lateral luxations, and avulsions result in greater incidence of pulp necrosis and resorptions. Indeed, depending on the type of luxation injury, an immature permanent tooth would become necrotic 14% to 67% of the time.[31] If an immature permanent tooth is avulsed and replanted, the risk of pulp necrosis is as high as 77%.[34] Therefore dental trauma is a major cause of interruption of tooth development because the dental pulp is readily infected and becomes necrotic in immature permanent teeth.

Caries

Dental caries is one of the most common infectious diseases in children and young adults, with high prevalence in the United States.[35,36] The National Health and Nutrition Examination Survey (NHANES) showed a decrease in its overall incidence, although 21% of children (6 to 11 years old) continue to have dental caries on permanent teeth, with 8% of children having untreated decay. Approximately 59% of adolescents (12 to 19 years old) and 92% of adults (20 to 64 years old) have dental caries in their permanent teeth. Untreated decay affects 20% of adolescents and 26% of adults.[37-39] The incidence and rate of progression of dental caries are multifactorial, depending on genetics, diet, and oral hygiene habits.[35] The lack of prompt treatment for carious lesions and/or the resulting microleakage from defective restorations leads to pulpitis, which can eventually progress to pulp necrosis, periapical lesions, infection dissemination, and systemic involvement, with eventual tooth loss. Therefore early treatment is crucial to maintain the vitality of the pulp, especially in young patients with immature teeth undergoing development. In active caries lesions, it is important to differentiate the infected from affected dentin. As discusses previously, indirect or direct pulp capping procedures can be employed after adequate caries excavation, allowing for remineralization of affected dentin or formation of a new mineralized bridge.[40-43]

Dental Anomalies

Dental anomalies such as dens evaginatus, dens invaginatus, or radicular lingual or palato-gingival groove are less frequent etiologic factors but can also cause pulpal necrosis. In these conditions, bacteria will have a direct access to the pulp through the malformations. Dens evaginatus, which is an occlusal tubercle formed during development by folding of inner enamel epithelium into the stellate reticulum, is most commonly found in mandibular secondary premolars.[44] Dens evaginatus has been reported to be prevalent in 1% to 4% of Asian populations and up to 15% in Alaskan Yupik and Inupiat people and North American Indian population.[44-47] Dens invaginatus, on the other hand, is formed from in-folding of the inner enamel epithelium and odontoblast layer into the pulp. The highest incidence of dens invaginatus is observed in maxillary lateral incisors, and the overall prevalence has been reported as 1% to 10%.[45,48,49] Oehlers has classified this anomaly by the degree of invagination affecting either the periodontium, pulp canal space, or both.[50] The pulp is exposed, in the most severe cases, when the communication passes directly to the apical papilla, communicating with the apical third of the canal and giving a direct entrance for bacteria. The radicular lingual grooves, similarly to dens invaginatus, are mostly found in lateral incisors and less common in central incisors.[48,50]

Iatrogenic Factors

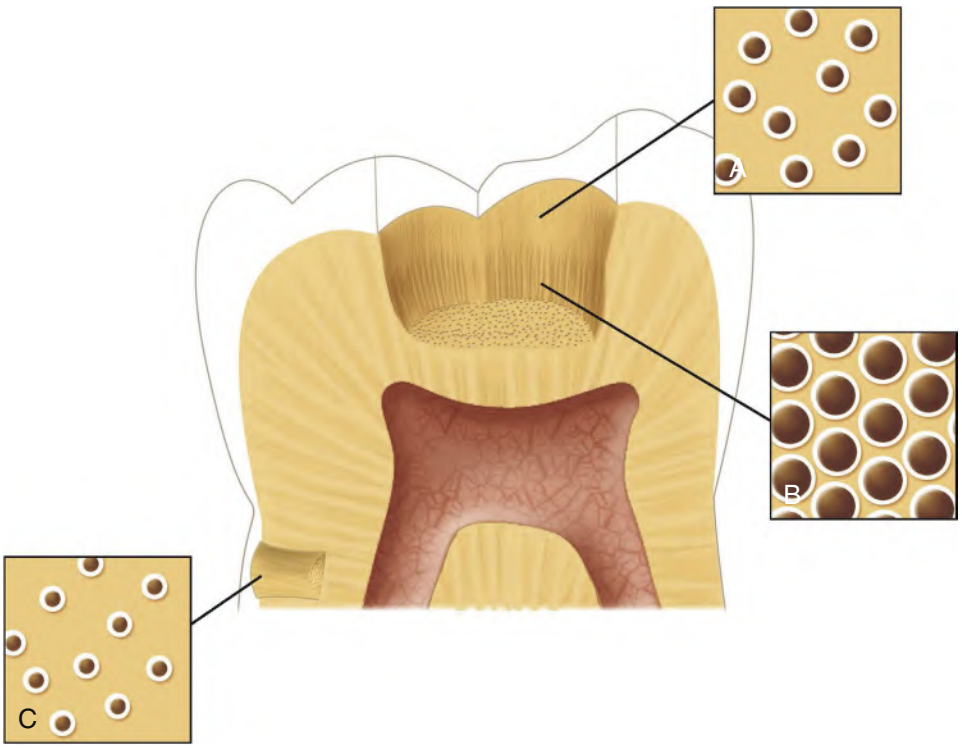
Cavity Preparation Aspects and Remaining Dentin

The blood flow to the pulp is reduced to less than half its normal rate when local anesthetics containing vasoconstrictors are used

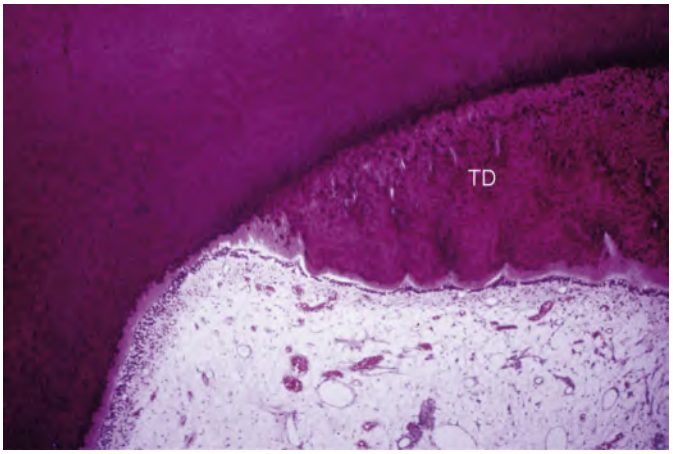
in restorative dentistry.[51] In procedures on teeth with pulps that are already compromised, this reduction may be an additional stressor. A healthy pulp may survive episodes of ischemia lasting for 1 hour or longer.[52] An already ischemic pulp subjected to severe injury may hemorrhage (blush) when subjected to trauma such as that associated with full crown preparation without the use of coolant.[53] Any intervention that extends to the dentin during cavity preparation may result in some degree of injury to the odontoblasts and their processes. However, dentin matrix demineralization during the carious process of cutting and etching of the dentin during cavity preparation can lead to release of important bioactive molecules, with the consequent stimulation of reparative cellular responses in the pulp.[54,55] Dentin is an effective insulator; for this reason, careful cutting with adequate cooling is less likely to damage the pulp unless the thickness of the dentin between preparation and pulp is less than 1 mm.[56] Even then, the inflammatory response may be mild (Fig. 10.6). The greatest amount of frictional heat is generated during crown preparations when the pulp is particularly at risk of injury. The heat generated may also have a desiccating effect by "boiling" away dentinal tubule fluid at the dentin surface. The "blushing" of dentin during cavity or crown preparation is thought to be due to frictional heat, resulting in vascular injury (hemorrhage) in the pulp.[57] Dentin may take on an underlying pinkish hue soon after a operative procedure, reflecting significant vascular changes that could result in the development of pulpitis. Thus crown preparation must be performed with adequate use of profuse water spray with new sharp burs and minimizing the pressure of the instrument on the tooth and the time of contact. In addition, it is imperative to establish the preoperative and postoperative pulp status through vitality testing.

Dentin permeability increases exponentially with increasing cavity depth, because both the diameter and density of dentinal tubules also increase with cavity depth (Fig. 10.7).[58,59] Thus the deeper the cavity, the greater the tubular surface area into which potentially toxic substances can penetrate and diffuse to the pulp. The length of the dentinal tubules beneath the cavity is also important. The farther substances diffuse, the more they are diluted and buffered by the dentinal fluid. Deeper cavity preparations sever the odontoblast processes in their region of greater length.

• **Fig. 10.6** Mild inflammation beneath a deep cavity preparation with adequate coolant. (Courtesy Dr. H.O. Trowbridge.).



• **Fig. 10.7** Difference in size and number of tubules in the dentinal floor of a shallow **(A)**, deep **(B)** and cervical **(C)** cavity preparations. (From Trowbridge HO: Dentistry today, *Dentistry* 82:22, 1982.)



• **Fig. 10.8** Tertiary dentin (TD) formed under a deep preparation and irritating material. (Courtesy Dr. H.O. Trowbridge.)

This severing negatively affects the cell's attempts to restore its membrane integrity and increases the risk of a cell leaking its contents.

Dental Materials

The most important characteristic of any restorative material on its effect on the pulp is its ability to form a seal that prevents the leakage of bacteria and their products onto dentin and the pulp.[60-63] Cytotoxicity is another important factor to evaluate in the restorative materials, because they are composed of chemicals that have the potential to irritate the pulp. However, when these materials are placed in a cavity, the intervening dentin usually neutralizes or prevents leachable ingredients from reaching the pulp in a high enough concentration to cause injury. Materials are more toxic when they are placed directly on an exposed pulp. Cytotoxicity tests carried out on materials in vitro or in soft tissues may not predict the effect of these materials on the dental pulp. The toxicity of the individual components of a material may vary.[64,65] A set material may differ in toxicity from an unset material. The immediate pulpal response to a material is much less significant than the long-term response. A few days after placement, the pulp may show a strong inflammatory response. A few months later, the inflammatory response may subside, and repair occurs. A good measure of long-term response is the thickness of tertiary dentin laid down by the affected pulp (Fig. 10.8). As discussed previously in this chapter, new bioactive silicate materials have been found by numerous studies to promote healing of the injured pulp by reparative and regenerative processes.

Vital Pulp Therapy

Maintenance of pulp vitality should always be the goal in treatment planning, and considerable interest is developing in the concept of regenerative endodontics for complete or partial pulp tissue regeneration. This interest in maintaining the biological functions of the dental pulp and the recognition that they are important for the longevity and overall health of the patients dates back to 1756 with the original attempts of pulp capping.[66] The introduction of calcium hydroxide[67] and more recently, the widespread use of hydraulic tricalcium silicates such as mineral trioxide aggregate (MTA; Dentsply, York, Pennsylvania, USA), Biodentine™ (Septodont, Saint-Maur-des-Fossés, France) and Endosequence® RRM™ (Root Repair Material) (Brasseler, USA) among others[68,69] have all emphasized the central role for biologically based therapies in endodontics. In general, vital pulp therapies can be classified in two broad categories: capping procedures and pulpotomies. These procedures differ in degrees of invasiveness and largely depend on the clinician's assessment of the extent of contamination and pulpal inflammation. This subjective assessment is performed chairside and relies on accurate clinical testing and diagnosis based on the signs and symptoms of disease and direct inspection of residual dentin and/or pulpal tissue under high-power magnification and illumination. Once vitality has been confirmed clinically by pulp sensitivity tests such as the application of cold or electrical pulp testing (EPT), careful inspection of the residual healthy tissue must be performed. Hemorrhage or lack thereof is often used as an indicator of the level of inflammation in the dental pulp. Continued bleeding despite application of mild pressure by an operator is interpreted as pulp that is too severely inflamed to be directly capped. Instead, more of the pulp tissue must be removed until its healthy appearance is observed and hemostasis is achieved. Although there have been attempts to develop methods to determine the level of inflammation of the residual pulp tissue based on biomarkers,[70] these methods have not yet been fully validated and are not immediately available for clinicians. Thus clinicians still rely on their expertise and subjective assessment when determining which vital pulp therapy is most suited for each particular case.

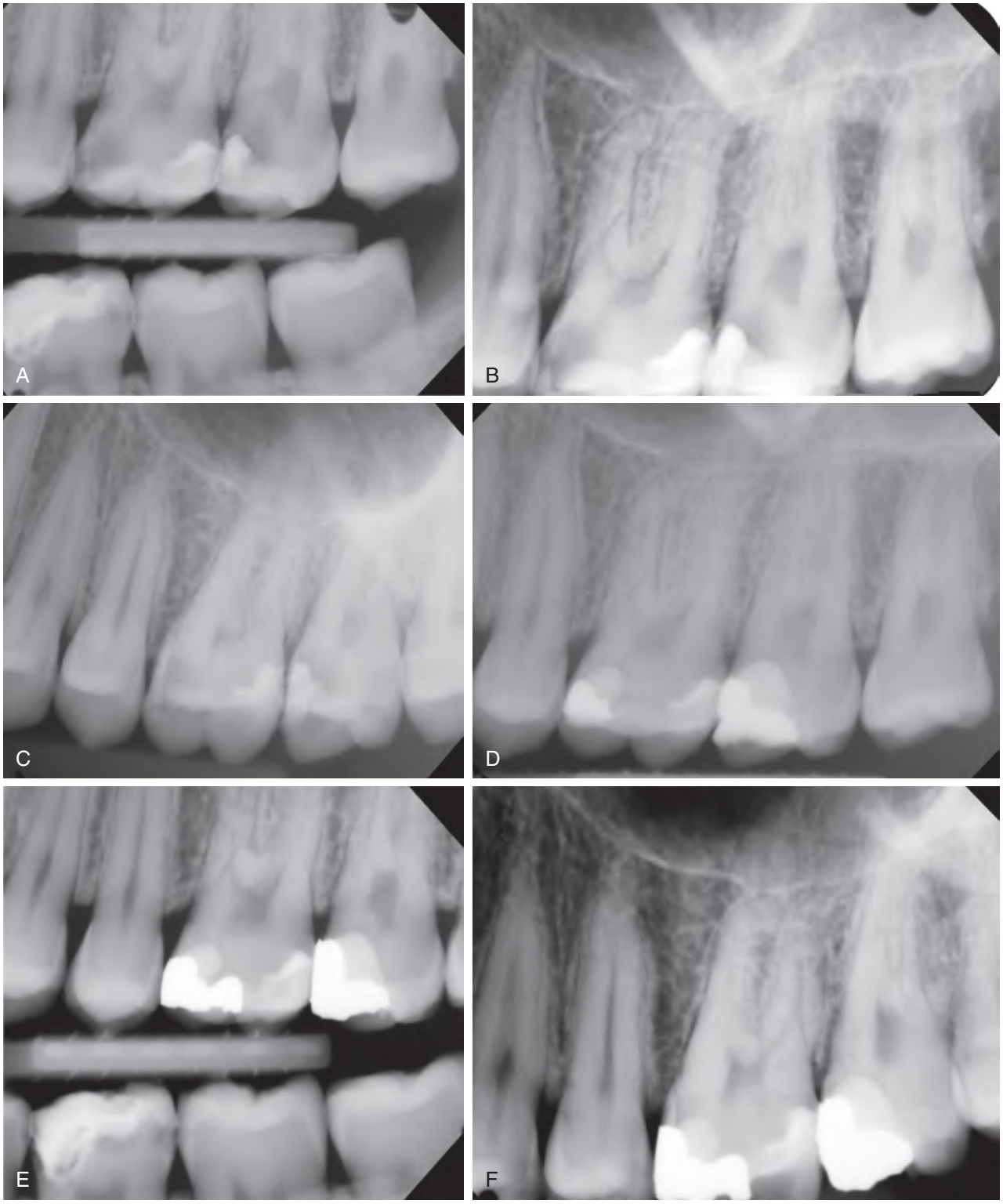
Capping Procedures

Indirect Pulp Capping

A clinician must always first identify the etiology of the insult and reach an accurate diagnosis. In the case of caries or uncomplicated crown fractures (without pulp exposure), excavation of infected dentin and cavity disinfection must be first achieved. If possible, the pulp tissue should not be violated. This goal can be achieved by progressive removal, using caries indicator to detect contaminated dentinal tissue. It has been shown that cavity preparations with residual dentin thickness of at least 0.5 mm from the pulp could be successfully capped with a bioactive material, resulting in the desirable formation of reactionary dentin, particularly in young patients.[71] This capping approach is called *indirect pulp capping* because the bioactive material does not directly contact the pulp tissue. Yet its bioactive components and high pH can neutralize bacteria[72,73] and their antigens and directly stimulate odontoblasts to produce reactionary tertiary dentin in the site of injury.[74] Ideally, the bioactive materials are placed over residual healthy, uninfected dentin. However, there is evidence that residual softened dentin can be capped, still resulting in tertiary dentin and arrested progression of the disease with the use of these materials.[74] This partial caries removal approach can be accomplished in one visit or may be followed by additional visits for excavation followed by capping, called *step-wise caries excavation*.[75,76] These conservative approaches strongly rely on the remineralization of the residual dentin and further formation of tertiary dentin by a healthy pulp. Therefore clinicians need to maintain a close follow-up to ensure that these biological goals are being achieved and that the pulp remains vital and the patient asymptomatic (Fig. 10.9).

Direct Pulp Capping

The exposure of the pulp tissue without major contamination can happen upon mechanical exposure of the dental pulp by trauma or during cavity preparation. In this instance the pulp may be



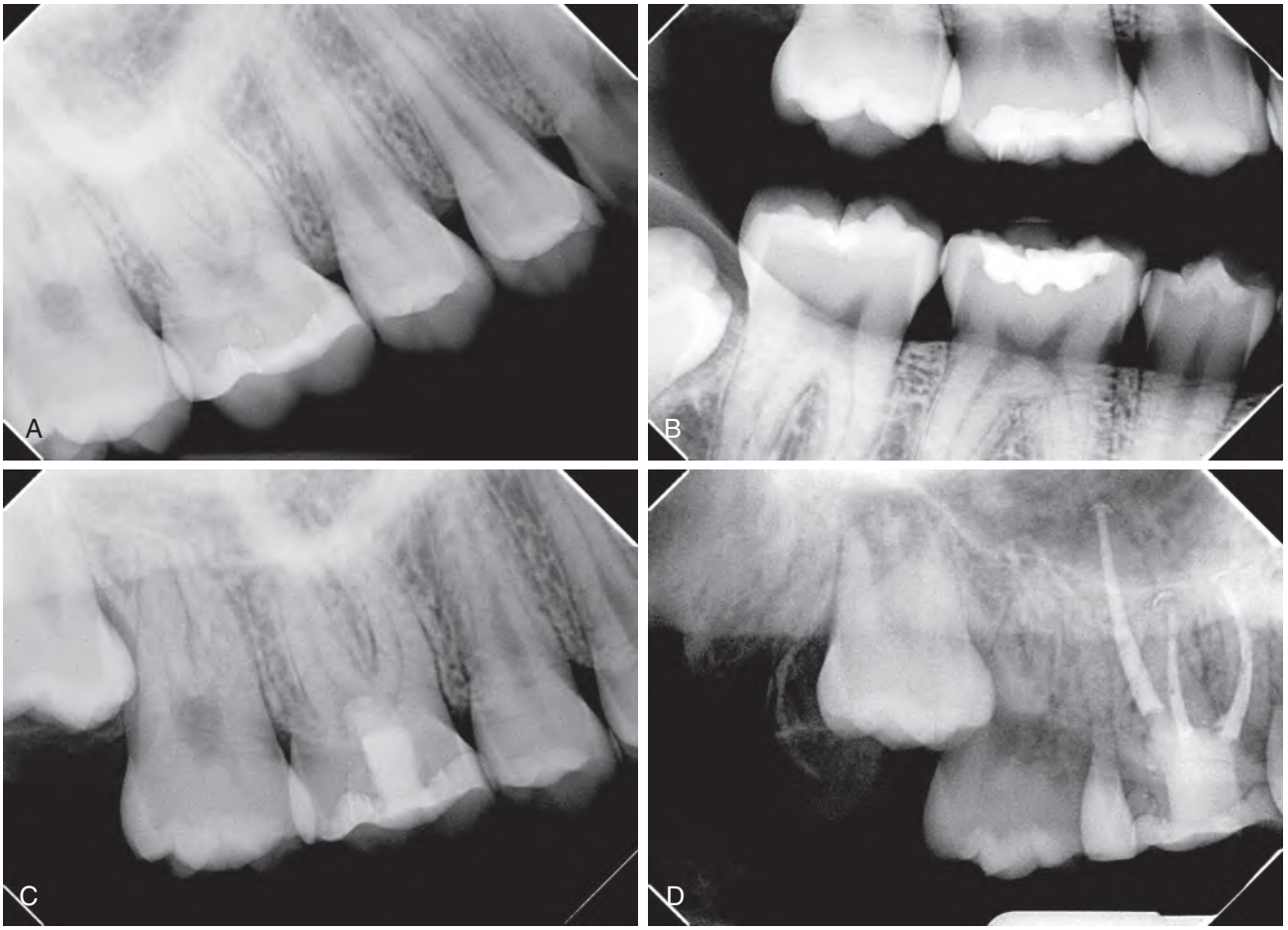
• **Fig. 10.9** An 18-year-old male patient with asymptomatic deep caries lesions on #14 and #15 and diagnosed with reversible pulpitis and normal periapical tissues diagnosed (**A**, **B**, and **C**). Caries were removed and indirect pulp capping performed on both teeth under rubber dam isolation with Biodentine™ (Septodont, Saint-Maur-des-Fossés, France) and coronal seal with Fuji IILC (GC America), followed by an amalgam final coronal restoration (**D**). At 1-year follow-up, tooth was asymptomatic and was diagnosed with normal pulp and normal periradicular tissues (**E** and **F**). (Case courtesy Dr. Tatiana M. Botero, private practice, Alsip, Illinois, USA.)

protected and its vitality maintained by immediately covering it (pulp capping) with a bioactive material and placing a restoration, thereby avoiding root canal treatment. This approach has been shown to have an excellent prognosis in incompletely formed teeth but has also been shown successful in permanent teeth with fully formed roots. However, in cases of long-standing carious exposure of the pulp, lower success rates are expected when a direct pulp-capping procedure is performed.[77] Recently, new data on the regenerative potential of the dental pulp and the development of newer bioactive materials have broadened the effectiveness of direct pulp-capping procedures.

Pulpotomies

If the exposure is large or seriously contaminated, it may require the removal of the superficial layer of the diseased pulp (partial pulpotomy) or the entire coronal pulp to the level of the root canal orifice (pulp chamber pulpotomy). As with direct pulp capping, close follow-up is recommended to ensure that, if needed, appropriate further treatment is provided in a timely fashion (Fig. 10.10).

Partial pulpotomies (also known as *Cvek pulpotomies*)[78] rely on the removal of the superficial most layer of infected or irreversibly injured pulp, followed by the direct capping of the residual healthy pulp. This technique relies on the subjective clinical assessment of inflammation upon direct visualization of the tissues. This assessment is best achieved with the use of the operating microscope that facilitates the visualization of hemorrhagic parts of the dental pulp. Typically, a pulp is considered irreversibly inflamed if it bleeds profusely despite local hemostasis measures. In these instances, the clinician may elect to remove more of the pulp or the complete removal of the pulp in the chamber to the level of the canal orifices (pulp chamber pulpotomy). In brief, the affected tooth is adequately isolated with the dental dam, and the infected

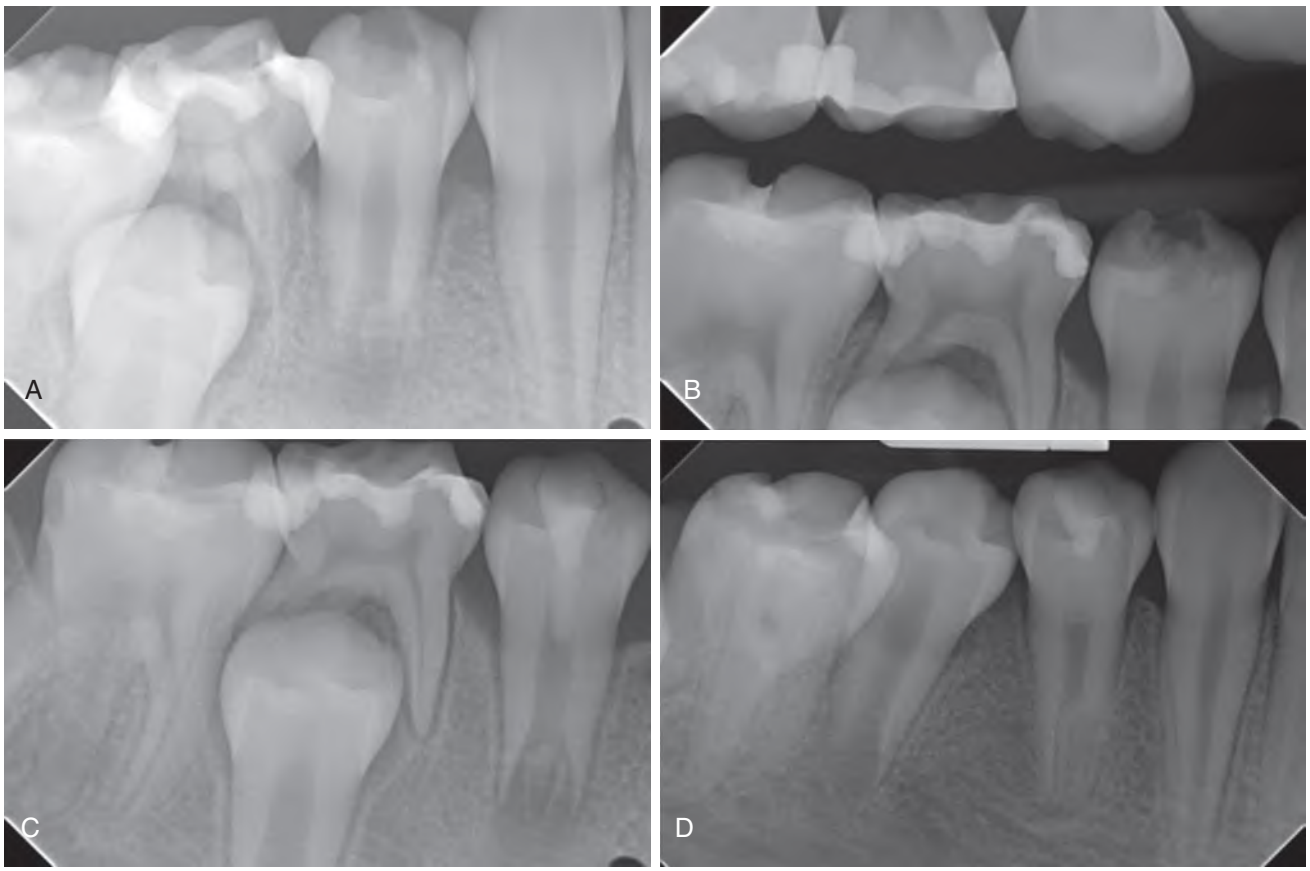


• **Fig. 10.10** A 16-year-old female presents to clinic with a chief complaint of pain in the upper right tooth. Tooth #3 was restored 4 months before with an occlusal composite restoration. Patient reported pain triggered by hot, cold, and chewing but she was not experiencing spontaneous pain or pain that woke her up at night (**A** and **B**). Vital pulp therapy was completed under rubber dam isolation. The pulp chamber was accessed, coronal pulp tissue removed, and hemostasis achieved with less than 5 minutes of a sodium hypochlorite (NaOCl)-soaked cotton pellet pressure. Biodentine™ was placed in the pulp chamber, and restoration completed with Fuji II LC and composite core build-up material **(C)**. Patient returned 4 weeks later with throbbing pain triggered by hot and chewing, which had started 2 weeks earlier. Nonsurgical root canal treatment was completed under rubber dam isolation, obturation completed with gutta-perch and Roth's sealer. Tooth was restored with glass ionomer and core build-up material **(D)**. Patient was asymptomatic 2 months post-non-surgical root canal therapy (NSRCT). (Case courtesy Dr. Sukhpreet Sandhu, Advanced Program in Endodontics at the University of Texas Health at San Antonio, San Antonio, TX, USA.)

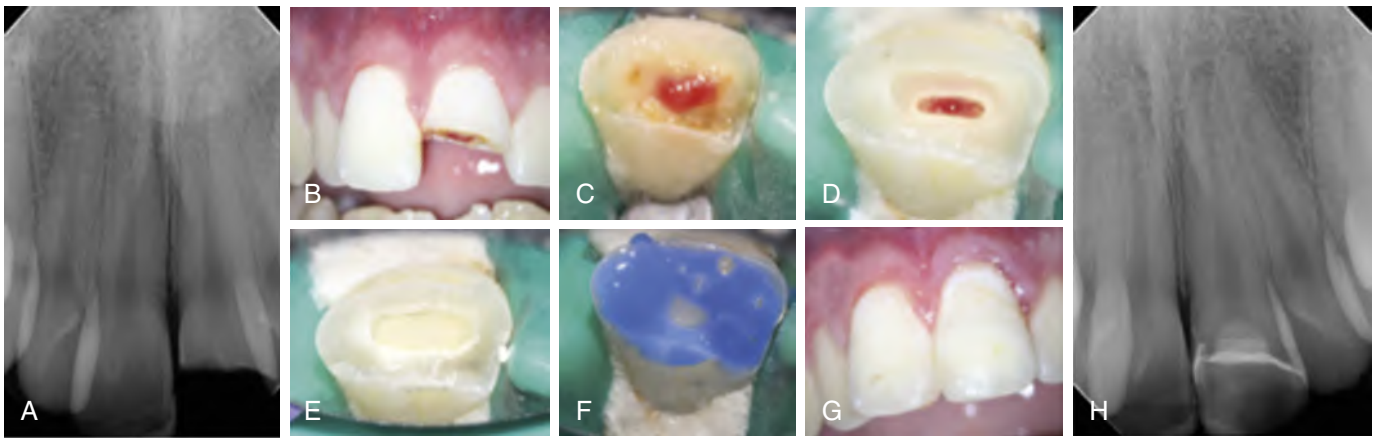
dentin and damaged pulp is removed with water-cooled diamond bur at high speed. Next, a cotton pellet soaked in sodium hypochlorite is placed over the pulp with gentle pressure, followed by 17% ethylenediaminetetraacetic acid (EDTA). After the cavity is dried, a tricalcium silicate material is placed over the pulp/dentin, followed by a final coronal sealing restoration. Partial pulpotomies, when performed with good aseptic techniques and using bioactive silicate materials, demonstrate excellent success rates, allowing root maturation (maturogenesis) and normal physiologic responses[79] (Figs. 10.11 and 10.12).

A complete pulp chamber pulpotomy is often required when the coronal pulp is heavily inflamed or with a questionable vitality status. Once the pulp in the chamber is removed under rubber dam isolation with a diamond bur at high speed with plenty of sterile water as coolant, a cotton pellet soaked in sodium hypochlorite is placed over the pulp stump(s) and gentle pressure is applied for 2 to 5 minutes. This technique allows for disinfection and hemostasis (if not irreversibly inflamed), which should result in pulp stumps with minimal to no bleeding. Next, the chamber is quickly rinsed with 17% EDTA and gently air dried, and a layer of >4 mm of a bioactive tricalcium silicate material is placed over the pulp stumps. Finally, the tooth is sealed with a definitive restoration (e.g., composite restoration). Patients should be reevaluated at 6 and 12 months, followed by annual evaluations for the first 4 years. This procedure has been shown to have excellent clinical results, promoting the maintenance of vitality, continued root development, and the lack of symptoms, and it may be considered definitive treatment in certain cases[80] (Figs. 10.13 and 10.14).

It is important to recognize, however, that pulp inflammation is a progressive disease, and the use of regenerative approaches to maintain pulp vitality requires a good understanding of the interplay of biologic factors influencing regenerative events, in addition to appropriate case selection. Such approaches may not be suitable for all cases, especially those showing deep pulp inflammation involving the radicular tissue, and the correlation of clinical symptoms with the pathophysiologic status of the dental pulp remains a significant challenge. In addition, there are no studies evaluating the long-term outcomes of these procedures in large patient populations,[15] and patients should be evaluated closely to ensure that the biologic outcome of continued root development and vitality are being achieved, and conventional root canal therapies should always be considered if vital pulp therapies fail to achieve their biologic goals.



• **Fig. 10.11** A 10-year-old female patient was evaluated for pain upon mastication on tooth #28 for approximately 2 weeks. The tooth had occlusal caries and immature, partially formed root, and it was diagnosed as reversible pulpitis with normal periradicular tissues (**A** and **B**). A partial pulpotomy was performed under rubber dam isolation with Biodentine™ being placed over the vital pulp, followed by a glass ionomer and composite restoration **(C)**. At 1-year recall, the patient was asymptomatic, responded normally to vitality testing, and demonstrated the completion of development of a bifurcated root and normal periapical tissues **(D)**. (Case courtesy Dr. Saeed Bayat Movahed, Graduate Endodontics Program. University of Texas Health at San Antonio, San Antonio, TX, USA.)



• **Fig. 10.12** A 17-year-old male patient presented with a complicated crown fracture after trauma of tooth #9 approximately 24 hours before the appointment. A preoperative periapical radiograph **(A)** and clinical examination **(B)** confirmed the presence of a frank pulp exposure **(C)**. The tooth responded to vitality testing with an exaggerated but nonlingering response to cold test, and it was diagnosed as reversible pulpitis. Approximately 2 mm of the affected coronal pulp was removed under rubber dam isolation and hemostasis was achieved with topical application of 2.5% sodium hypochlorite (NaOCl) followed by 17% ethylenediaminetetraacetic acid (EDTA) **(D)**. A 3-mm-thick layer of Biodentine™ (Septodont, Saint-Maur-des-Fossés, France) was placed over the vital pulp **(E)**. The tooth was etched **(F)** and the fractured fragment kept by the patient was bonded and restored with composite **(G)**. A postoperative periapical radiograph revealed adequate coronal seal and adaptation of the fractured segment **(H)**. The patient has remained asymptomatic since the treatment. (Case courtesy Dr. Koyo Takimoto, Advanced Program in Endodontics at the University of Texas Health at San Antonio, San Antonio, TX, USA.)

Study Questions

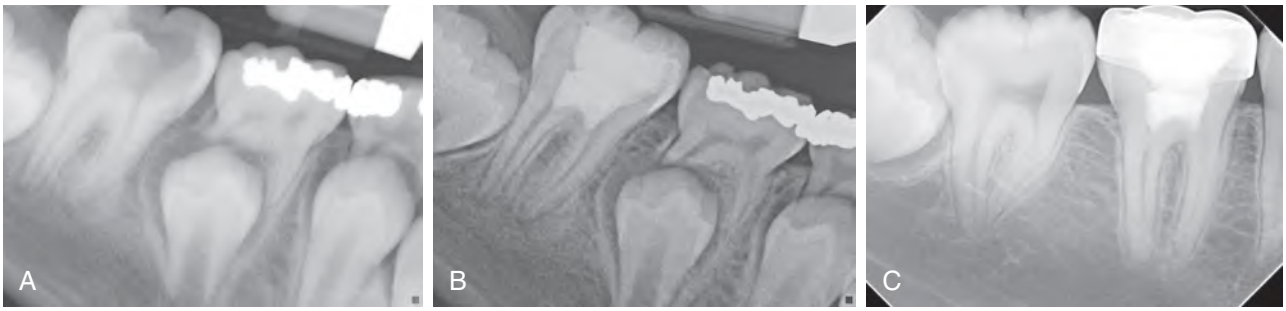
1. The following are defense mechanisms of the dental pulp:
   a. Outward fluid flow
   b. Neurogenic inflammation
   c. Arteriole/venule (A/V) shunt
   d. Tertiary dentinogenesis
   e. All of the above
2. The following is NOT an example of vital pulp therapy:
   a. Partial pulpotomy
   b. Full chamber pulpotomy
   c. Pulpectomy
   d. Direct pulp capping
   e. Indirect pulp capping
3. The following is true regarding partial or complete pulp chamber pulpotomies:
   a. Use of bioactive dental materials is advocated.
   b. They are considered only temporary therapies.
   c. They have considerably lower success rates compared with nonvital therapies.
   d. Teeth diagnosed with pulp necrosis can benefit from these procedures.
4. What are the most common teeth affected by traumatic injuries?
   a. Anterior maxillary
   b. Anterior mandibular
   c. Posterior maxillary
   d. Posterior mandibular

Treatment of Immature Teeth with Pulp Necrosis

Immature teeth with pulpal necrosis present clinical challenges due to persistent infection in the root canal system, often associated with periradicular bone loss and inability to effectively disinfect the root canals and seal the root canal space. These cases are exemplified in premolars with dens evaginatus, a form of enamel defect at the occlusal surface resulting in pulpal exposure after abrasion of the occlusal enamel.[46] Necrotic changes in the pulp after exposure in dens evaginatus often occurs in pediatric patients with incomplete root development and open apices.[81] Alternatively, pulpal necrosis can occur in any permanent teeth from carious lesions that have penetrated through the dentinal layers to cause the root canal infection at any stage of root development. Endodontic treatment of immature teeth with pulpal necrosis is vastly different from vital pulp therapies. In cases of infection, the focus is on root canal débridement and control of infection, followed by sealing of the disinfected root canal space with artificial material, or an attempt to regenerate vital tissue. On the contrary, vital pulp therapies are primarily focused on preservation of the remaining vital pulp tissues, as seen in the cases of direct pulp capping or pulpotomies as described previously in this chapter. Thus this section of the chapter will discuss our treatment strategies for immature teeth with pulpal necrosis, which mainly include apexification and regenerative endodontic therapies.

Apexification—Indications, Approach, and Limitations

For immature teeth with pulp necrosis, root canal débridement can be accomplished with mechanical instrumentation and copious irrigation with antimicrobial irrigating solutions. Obturation of the root canal space is necessary to avoid remaining bacteria or microbial biofilm growth after the clinician's attempt to disinfect the root canal space. In particular, teeth with pulpal necrosis are generally considered infected with bacteria within the complexities of root canal space, including dentinal tubules, especially when radiographic lesions are visible. It has been shown that tubular infection with bacteria occurs rapidly after dentinal inoculation with the microorganisms and that the depth of tubular penetration



• **Fig. 10.13** An 11-year-old male with large carious lesion and diagnosis of reversible pulpitis **(A)** was treated with full pulp chamber pulpotomy performed with white mineral trioxide aggregate (MTA) (Dentsply, York, PA, USA) and a composite restoration **(B)** followed by a stainless-steel crown. At 7-year recall, the tooth is asymptomatic, responds normally to vitality testing and displays completion of root development and normal periradicular tissues **(C)**. (Case courtesy Dr. Tyler Lovelace, Advanced Program in Endodontics at the University of Texas Health at San Antonio, San Antonio, TX, USA.)

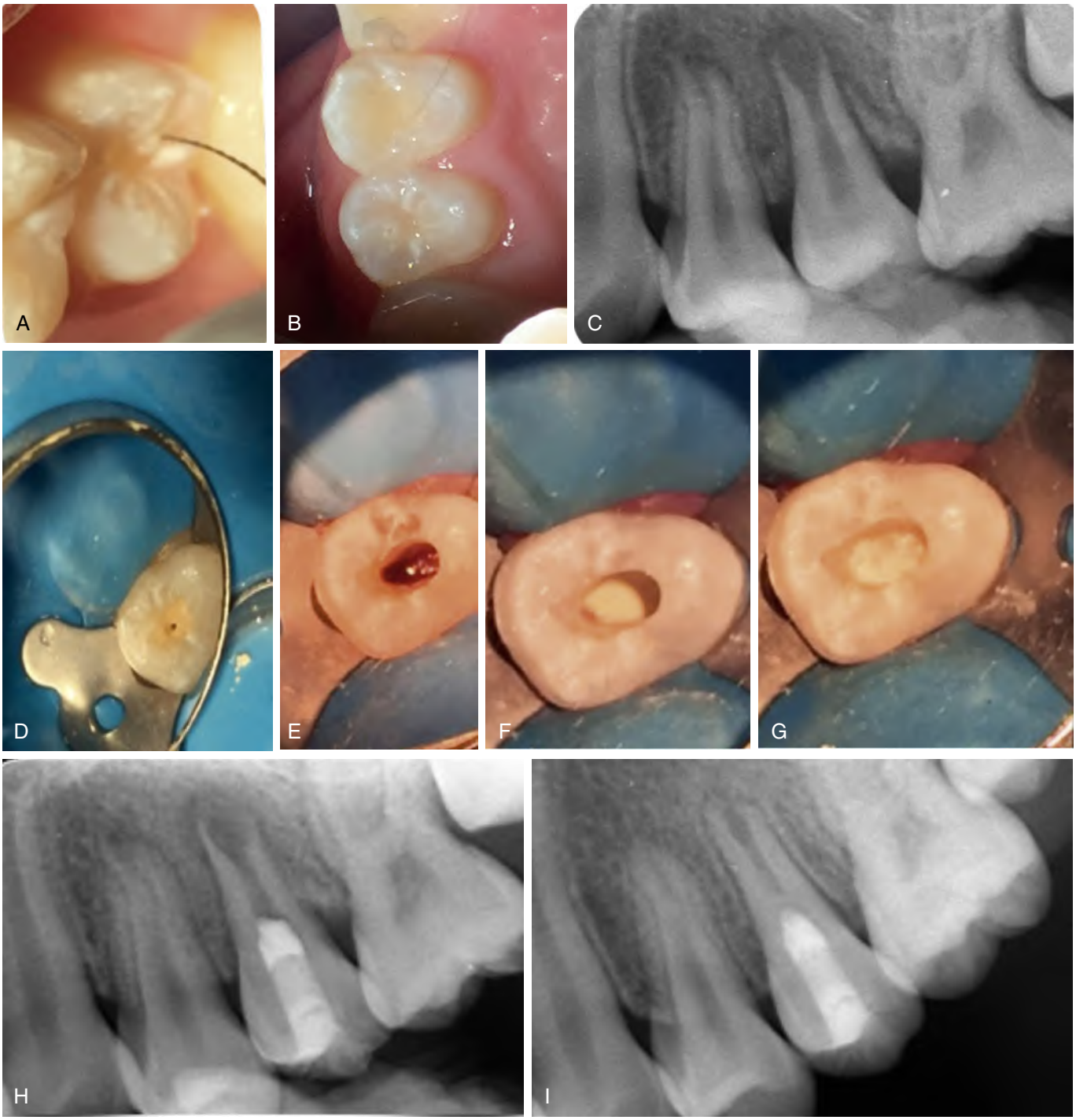
occurs in a time-dependent manner.[82] Hence in cases in which the apical constriction has not yet been formed, the obturation of the root canal system can be accomplished by a procedure called *apexification*. In these procedures, a calcific barrier is formed after long-term calcium hydroxide medicament or immediately with the use of an MTA or other tricalcium silicate as an apical plug.

Apexification is different from apexogenesis (Video 10.1), which is accomplished with vital pulp therapies. In apexification, no vital pulp tissue is preserved because root canal obturation will occur to the most apical extent of the root, regardless of the size of the apical opening. Thus no further root development is anticipated in teeth treated by apexification, whereas apical closure and further root development is anticipated in those treated by apexogenesis. Studies have clearly demonstrated that immature teeth treated by apexification do not undergo changes in the root dimension, such as lengthening or thickening of the root dentin.[83-87] Conceptually, apexification has as its primary goal apical closure, which can be accomplished by an indirect approach using $Ca(OH_2$ as intracanal medicament or directly by placement of MTA or other hydraulic silicate cement to the apical extent of the root canal space. The $Ca(OH)_2$-mediated apical closure formation is an indirect approach because it relies on the establishment of a hard tissue apical barrier, which often requires an extended period of $Ca(OH)_2$ medicament and multiple appointments.[88] Typically, $Ca(OH)_2$-mediated apical plug formation requires 3- to 9-month period of treatment, during which time the $Ca(OH)_2$ medicament needs to be replaced periodically, thereby requiring multiple patient visits. In addition, there is increasing evidence that long-term calcium hydroxide treatment can weaken dentin,[89,90] resulting in increased susceptibility to fractures.[91] These aspects are the major shortcomings of apexification with $Ca(OH)_2$ intracanal medicament. On the contrary, MTA (or other tricalcium silicate cements) apexification is a direct approach that does not require prior hard tissue formation induction; instead, an apical barrier as collagen plug followed by a bioactive cement will provide immediate apical barrier without the need for prolonged $Ca(OH)_2$ (Fig. 10.15). For this reason, apexification can be accomplished in a single visit (known as *one-step apexification*) without having to wait for the calcific barrier formation when the apical plug is established using MTA with same expected clinical success rate (Video 10.1).[92,93]

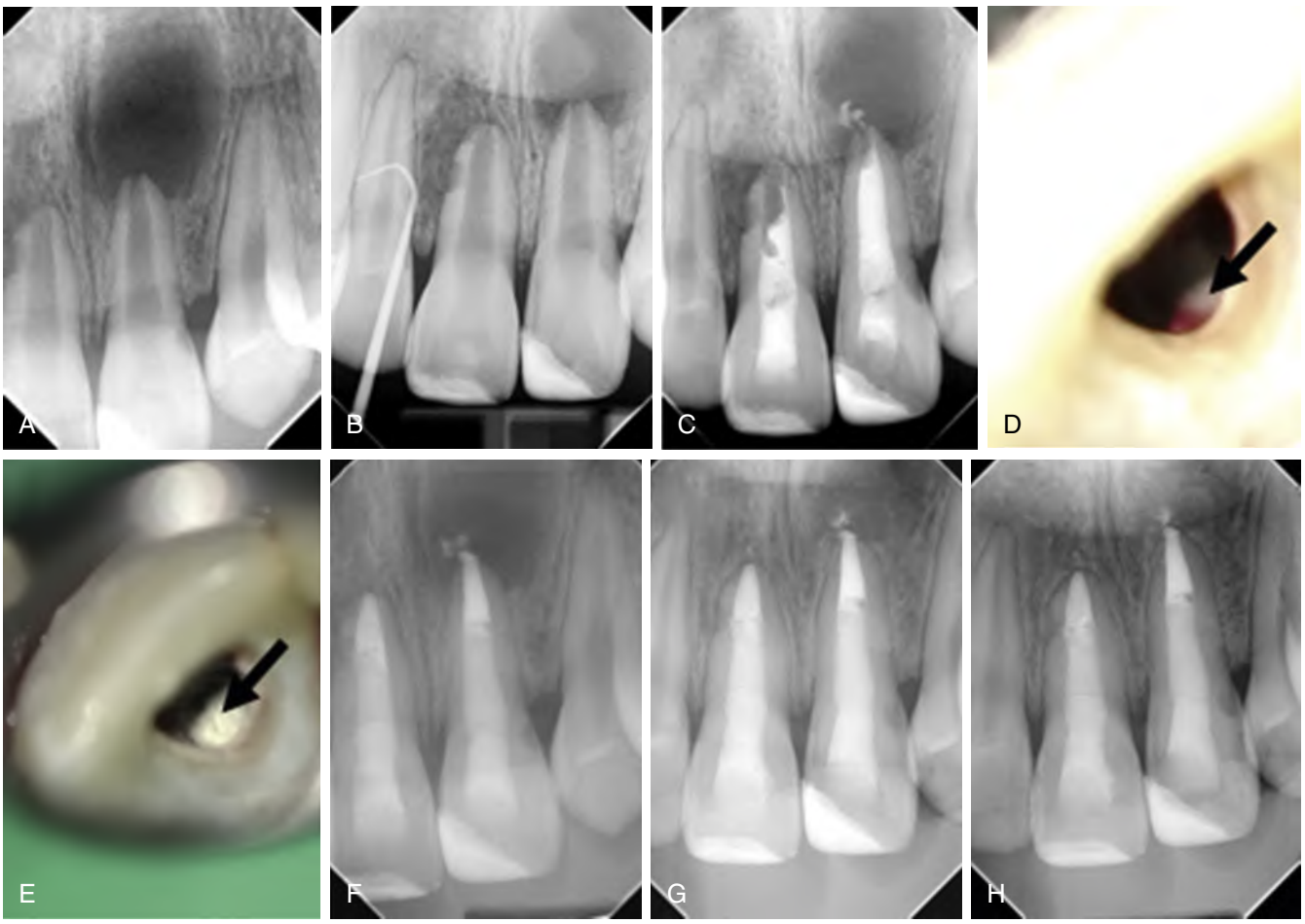
Apexification has been the treatment of choice for many decades for immature teeth with pulpal necrosis since the 1970s. A retrospective study involving 98 teeth treated with apexification showed greater than 90% success in terms of resolution of apical periodontitis over long-term follow-up period.[94] Other studies also demonstrated close to 100% success in resolution of apical periodontitis by apexification for teeth with open apices.[95,96] However, one of the main limitations of apexification is arrest of root development posttreatment, when the treatment is rendered in immature teeth with large open apex, underdeveloped root structures with thin and short root dentin. Consequently, there is increased probability of root fracture in immature teeth treated by apexification. When teeth with immature root development were treated and maintained after root canal filling, the incidence of cervical root fracture was significantly higher than those of mature-root filled teeth and depended on the stage of root development.[91] Thus cervical root fracture remains a plausible risk factor for those immature teeth treated by apexification, primarily because of absence of root dentin development despite resolution of apical periodontitis.

Apexification—Clinical Protocols

The clinical procedure for apexification varies among clinicians but may be accentuated as following, as previously described by Kang and Bogen.[97] Under profound local anesthesia, access is made using a #2 long-shank round bur, and root canals are débrided with hand instrumentation with larger K-files, primarily by circumferential filing due to enlarged lumen of the root canals. Passive irrigation of root canals may proceed with 1.5% sodium hypochlorite (NaOCl) for 15 to 20 minutes while performing the canal instrumentation. For patients that present with soft tissue swelling around the buccal gingiva or with draining through the sinus tract, intracanal medicament using $Ca(OH)_2$ is necessary with temporization with a cotton pellet and temporary restoration. Subsequently, after confirming the resolution of the soft tissue lesions, placement of MTA into the root canal apex may proceed, with drying the canals using extra-coarse paper points. In certain cases, a collagen membrane (e.g., CollaPlug™ or CollaTape™, Zimmer Dental Inc, Warsaw, Indiana,USA) can be placed in contact with the periradicular tissues at the apex to serve as internal matrix to prevent or minimize the extrusion of MTA into the periradicular tissues. Apical condensation of MTA using the back end of paper points or gutta-percha points may be necessary to ensure the material adaptation to the most apical extent of the divergent root canal apices. Radiographs should be taken to confirm the adequate placement of the apical MTA plug to assess the density and thickness of the apical plug. After at least 5 mm of apical plug is established, ensuring adequate apical seal, the coronal root canal space may be filled with either MTA or flowable gutta-percha, depending on the clinical needs



• **Fig. 10.14** An 11-year-old female patient with tooth #13 diagnosed with pulp necrosis and history of swelling. **(A)** A file could be placed in the communication between the pulp and the oral environment created by the dens evaginatus. **(B)** The opening of the tubercle is seen on the occlusal surface of tooth #13 *(black arrow)*. **(C)** Periapical radiograph revealed the presence of an immature root with thin dentinal walls and open apex. **(D)** Upon accessing through the dens communication, a vital pulp was seen under high magnification. **(E–G)** A full pulpotomy was performed with placement of Biodentine™, glass ionomer, and a composite coronal seal **(G, H)**. **(I)** At 1-year follow-up, the patient was asymptomatic, and radiographic examination revealed a mineralized bridge formation under the Biodentine™ and evidence of further root maturation with closure of the apex and normal periradicular tissues. (Courtesy of Dr. Tatiana M. Botero and Dr. Anna DeGraft-Johnson, Graduate Endodontic Program, University of Michigan, Ann Arbor, MI, USA.)



• **Fig. 10.15** A 16-year-old male patient with history of trauma to the anterior teeth due to a car accident 9 years prior has the chief complaint of intermittent pain, swelling, and intraoral drainage **(A)**. Intraoral examination revealed a sinus tract that was traced with a gutta-percha cone to tooth #8, which was diagnosed with pulp necrosis and chronic apical abscess; periradicular inflammatory root resorption is also observed on the periapical radiograph (**A** and **B**). Tooth #9 was diagnosed with pulp necrosis and symptomatic apical periodontitis due to lack of responses to vitality testing and the extreme tenderness to percussion and the large periapical radiolucency (**A** and **B**). On first visit, both teeth were accessed, and canals were débrided with Hedstrom files and irrigation with 6% sodium hypochlorite (NaOCl) and 17% ethylenediaminetetraacetic acid (EDTA), followed by placement of calcium hydroxide medicament for 1 month and access seal with Fuji Triage glass ionomer **(C)**. On the second visit (1 month later), the sinus tract had closed, and the patient was asymptomatic. Teeth were reaccessed, and canals were irrigated as in first visit. Next, a collagen membrane was placed at the apical foramen to prevent mineral trioxide aggregate (MTA) extrusion (*black arrow*; **D**). Next, white MTA was placed at apical one-third of each tooth (*black arrow*; **E**), and the canals were backfilled with thermoplasticized gutta-percha and accesses sealed a composite restoration **(F)**. At both 1-year **(G)** and 2-year recall **(H)**, both teeth were asymptomatic without swelling or sinus tract history with radiographic evidence of complete healing and arrestment of the resorptive process in tooth #8. (Case courtesy Dr. Anibal Diogenes, Endodontic Faculty Practice, University of Texas Health at San Antonio, San Antonio, TX, USA.)

and restorative plan for the tooth. Coronal restoration may be finalized using bonded composite material. Radiographic follow-up examination should be scheduled to assess resolution of apical periodontitis and absence of complications after 6 and 12 months postoperatively (Video 10.2).

Regenerative Endodontic Procedures (REPs)—Indications, Approach, and Limitations

In 2000 reports of isolation and characterization of multipotent adult stem cells from the dental pulp, namely dental pulp stem cells (DPSCs), had been published[98] followed by the identification of stem cells of the apical papilla (SCAP).[99] Shortly after, a case report demonstrated successful treatment of immature teeth with periapical abscess via regenerative approaches, which led to resolution of apical periodontitis and apical closure.[100] Those two findings have fueled the explosion of interest and research endeavors in regenerative endodontics, which led at least to an alternative treatment protocol for necrotic immature teeth through development of regenerative endodontic procedure (REP), also known as *pulp revascularization* or *pulp revitalization*. At present, REP is considered a viable treatment option for immature teeth with pulpal necrosis. This protocol presents critical advantages over apexification in that teeth undergo dimensional changes posttreatment

that result in increased root dentin thickness and length.[83,87] Consequently, REP is expected to address the major shortcomings of apexification, which are the arrest of root development and the permanent loss of pulp vitality.

The basic premise of REP is to allow indigenous mesenchymal stem cells (MSCs) around the periapex to continue the root development in the immature teeth by débriding the infected root canal space. The typical REP procedure involves disinfection of the root canal space by minimal instrumentation with antimicrobial irrigation and placement of medicaments (e.g., $Ca[OH]_2$ or triple antibiotic paste [TAP]), which includes metronidazole, ciprofloxacin, and minocycline, follow by coronal seal. In a second appointment, typically 2 to 4 weeks after the placement of medicament, indigenous MSCs from periapical tissues are recruited by means of induced bleeding into the root canal space[101,102] or placement of growth factor–enriched scaffold, such as platelet-rich plasma (PRP) or plate-rich fibrin (PRF), followed by capping material (MTA or other tricalcium silicate) and coronal restoration. Recent studies demonstrate successful REP through various clinical protocols.[96,103-106] The success/survival rate of REP in the literature is surprisingly high, nearing 100%, and successful outcome is defined by resolution of apical periodontitis.[96,104,105,107] Thus it is important to note that the success of REP in resolving apical periodontitis does not seem to depend on the variations of treatment protocols but is determined largely by successful disinfection of the root canal space, recruitment of MSCs, and biocompatibility of the coronal restoration. Whether the root canals were disinfected by $Ca(OH)_2$ medicament or mixture of antibiotics or whether the MSCs were recruited by induced bleeding[101,102] or placement of PRP/PRF,[108] no difference in the outcome has yet been seen.[109]

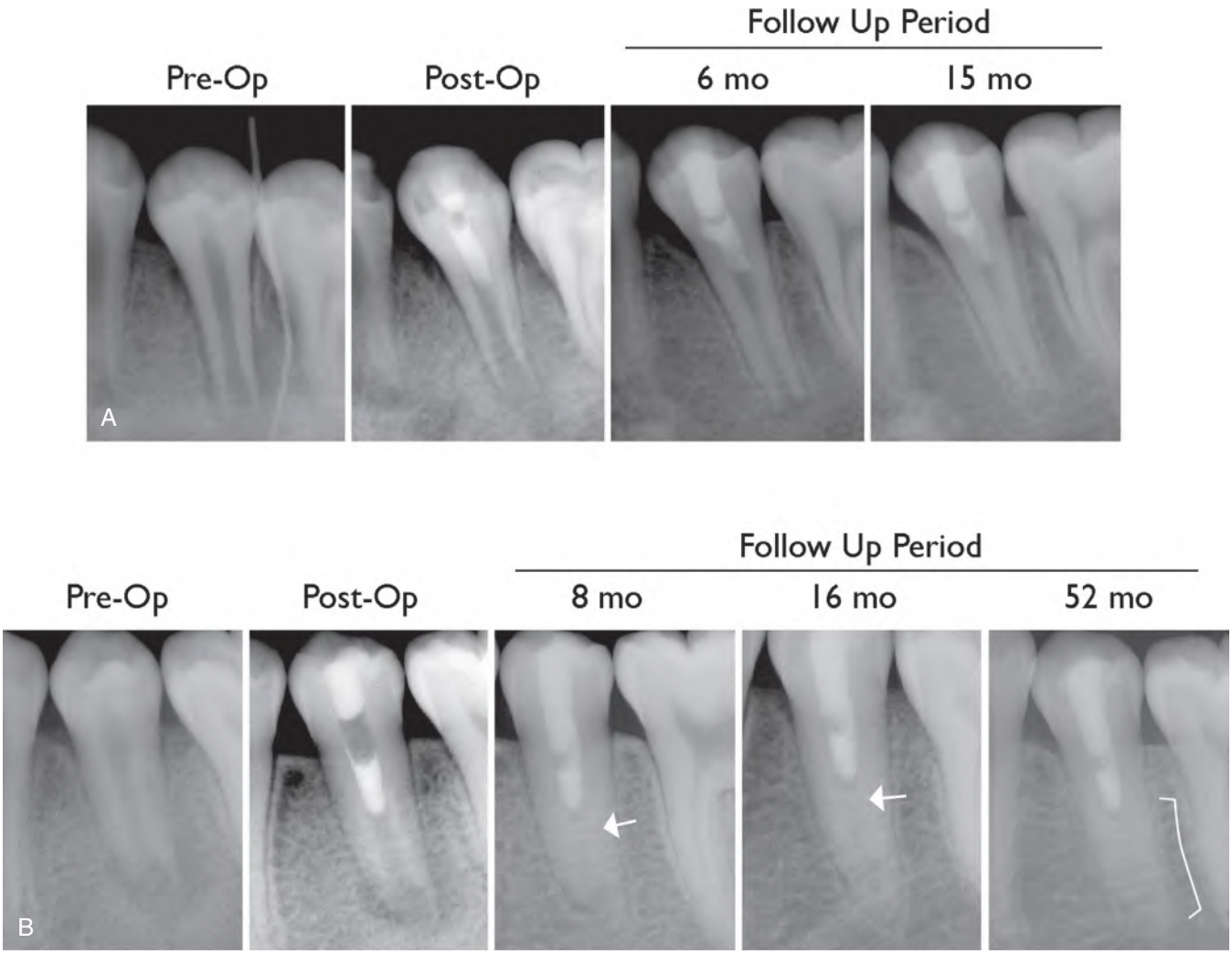
Although REP has clearly revolutionized how clinicians treat immature teeth with pulp necrosis, it falls short on de novo regeneration of the dentin-pulp complex with currently used techniques. Histologic studies on teeth treated by REP have revealed the absence of organized pulp tissues, such as a palisading odontoblast layer juxtaposed with the dentinal surface, and occurrence of ectopic tissue formation inside the lumen of root canals, which included bone, cementum, and fibrous tissues.[110] These findings were corroborated with large animal studies, which also revealed ectopic tissue formation in the root canal space after REP, in lieu of dentin-pulp regeneration.[111] Thus REP may represent "tissue repair" rather than de novo regeneration of functional dental pulp, although the procedure demonstrates efficacy in the resolution of apical periodontitis. These procedures have also been called "guided endodontic repair" (GER),[112] acknowledging the role of each clinical step of these procedures favoring formation of a vital tissue resembling the pulp as being a connective tissue with rich vascularity[113] and innervation,[114] but lacking the organization of the native dental pulp. The ectopic mineralization in the root canals after REP may manifest as rampant calcifications visible on the follow-up radiographs (Fig. 10.16). Song et al. recently reported the clinical outcome of 29 REP cases with varying clinical parameters and treatment protocols with 1- to 6-year recall period.[115] This longitudinal retrospective study also showed very high proportion of treatment success, with 80% of apical closures for those with open apices. Researchers were surprised to find that intracanal calcification was evident in 62% of REP cases to varying degrees, some with complete canal obliteration; REP cases that were followed at multiple time points revealed progressive increases in the level of canal calcifications. Hence, the so-called REP-associated intracanal calcification (RAIC) is a very common treatment complication and illustrates the major limitation of this treatment approach because RAIC could impede restoration of functional dental pulp after REP.

REP—Clinical Protocols

There are many variants of REP protocols that lead to successful treatment outcome. The American Association of Endodontists (AAE) has developed Clinical Considerations for Regenerative Procedures(https://www.aae.org/specialty/clinical-resources/regenerative-endodontics/), which outlines detailed protocols to be employed for REP. In addition, these treatment recommendations closely resemble those of the European Society of Endodontology (ESE).[116] In essence, the cases that would benefit from REP include immature teeth with pulp necrosis and adequate coronal tooth structure to be restored with direct restoration. Débridement of the root canal space may proceed with minimal instrumentation and irrigation with low concentration (1.5%) NaOCl, followed by intracanal $Ca(OH)_2$ or TAP dressing to resolve periradicular inflammation. The tooth is then temporarily restored until the second appointment. After confirming the absence of gross periradicular inflammation, such as resolution of soft tissue swelling or draining sinus tract, the tooth is ready for the second phase of REP, which involves recruitment of MSCs into the root canal space. The patient is anesthetized with a local anesthetic without vasoconstrictor, e.g., 3% mepivacaine, and the tooth is isolated with a rubber dam. After intracanal irrigation with 17% EDTA and visual confirmation of absence of draining exudate or necrotic debris, bleeding is induced into the root canal space by agitation of periapical tissues beyond the root apex, using small #10 K-files to allow the blood clot formation to the level of cementoenamel junction (CEJ). Collagen matrix, e.g., CollaPlug™ or CollaTape™, may be placed over the blood clot to provide a barrier onto which MTA or other tricalcium silicate can be placed as coronal capping material. In the final visit, the patient should be recalled for a 1-week postoperative check to confirm the absence of periradicular infection and resolution of the patient's symptoms. The tooth can then be restored with direct restoration (e.g., composite resin over MTA or other tricalcium silicate) (Fig. 10.17) and be followed up with a 6-month check, followed by yearly recall visits. Importantly, clinicians must become more familiar with this new treatment alternative and realize that the radiographic presentation of teeth treated with this treatment modality will appear as if endodontic the "filling" or obturation is missing. Therefore adequate treatment history and current vitality testing must be performed when history of this kind of treatment is suspected to prevent unnecessary re-treatment and the violation of a newly formed reparative vital tissue (Video 10.3).

Tissue Engineering Approaches

Although efficacious, REP presents limitations that involve ectopic tissue formation and calcification of the canal space, which may impede functional pulp regeneration. To circumvent these issues, pulp tissue engineering approaches have been developed and involve isolation, expansion, and transplantation of autologous pulpal MSCs. An earlier animal study revealed that de novo regeneration of the dentin-pulp complex requires transplantation of pulpal MSCs, whereas transplantation of scaffold alone led to ingrowth of fibrous tissues with no pulp tissue regeneration.[117] Likewise, a large animal study involving pulpectomy model in dogs showed successful



• **Fig. 10.16** Regenerative endodontic procedures (REPs) are efficacious in resolving apical periodontitis but with frequent occurrence of intracanal calcification. Tooth #20 is shown with large periapical radiolucency and gutta-percha tracing of sinus tract **(A)**. Due to open apex, regenerative endodontic therapy was performed, followed by coronal restoration with mineral trioxide aggregate (MTA). When the patient was recalled for 6-month follow-up, apical periodontitis had been completely resolved, and the tooth demonstrated complete closure of the apex. Also visible on the 6- and 15-month follow-up radiograph was lengthening and thickening of root dentin without evidence of intracanal calcification. **(B)** In a similar clinical scenario, tooth #20 presented with periapical radiolucency with open apex and was treated by REP and coronal MTA placement. In this case, REP successfully resolved apical periodontitis, but there is appearance of intracanal calcification at 8-, 16-, and 52-month follow-up, with progressive increase in the level of calcification with time after completion of REP (*arrows* and *bracket*). (Figures were modified from Martin G, Ricucci D, Gibbs JL, Lin LM: Histological findings of revascularized/revitalized immature permanent molar with apical periodontitis using platelet-rich plasma, *J Endod* 39(1):138–144, 2013.)

regeneration of whole pulp by transplantation of pulpal MSCs enriched with CD105+ immunophenotyped.[118] These animal studies demonstrated that functional pulp regeneration requires pulpal MSC transplantation, supporting the concept of cell-based approaches for endodontic regeneration. Recently a phase I clinical trial of MSC transplantation was performed successfully in patients presenting with symptomatic irreversible pulpitis.[119] This study tested the efficacy and safety of cell-based therapy, by which the investigators débrided coronal caries lesions, shaped the root canals, and transplanted autologous pulp MSCs into the root canal space mixed with a collagen scaffold. At successive evaluations, the investigators documented the resolution of patient symptoms, restoration of vitality and sensibility of pulp tissues, and absence of canal calcification in patients who received MSC transplantation in the root canal space. Hence, the cell-based tissue engineering strategy is feasible for endodontic regeneration and may circumvent the limitations of REP. Further research endeavors will focus on practicalities of cell-based endodontic regeneration to bring the technology chairside to benefit the public.

Conclusions

The dental pulp has elaborate defense mechanisms designed to minimize damage from microbial insults and trauma. Early intervention with minimally invasive procedures addressing the

• **Fig. 10.17** Regenerative endodontic procedure (REP) treatment protocol as recommended by the American Association of Endodontists (AAE) and European Society of Endodontology (ESE). At first appointment, after access and disinfection, the intracanal medication is placed and left for several weeks, rendering the root canal progressively more disinfected *(seen as color change in the illustration)*. At second appointment, the medication is removed, and bleeding is induced from periapical tissues. Blood clot is formed and capped with a collagen membrane and a tricalcium silicate cement (e.g., white mineral trioxide aggregate [MTA]; Dentsply, York, PA, USA or Biodentine™; Septodont, Saint-Maur-des-Fossés, France). Follow-up for 6, 12, and 24 months after treatment completion. Clinical case of an immature premolar with dens evaginatus and pulp necrosis at a 2-year follow-up. (Case courtesy Dr. Viraj Vora, private practice, Toronto, Canada. Graphics by Dr. Diogo Guerreiro, University of Michigan Ann Arbor, MI.) Figure was modified from Botero-D TM, Vodopyanov D, Degraft-Johnson A., Guerreiro D., "Procedures endodontiques regeneratives" Revue d'odonto stomatology. Tome 47, No 4, Dec 2018; 338-349.

etiology of the disease has the potential to favor regeneration and repair with excellent clinical prognosis. Advances in pulp biology and dental materials have played a fundamental role in improving outcomes of vital pulp therapies. Current and further knowledge gained on molecular markers of inflammation could result in better diagnosis and even more predictable outcomes. For the most severe cases of insult that resulted in pulp necrosis, the field of regenerative endodontics has made significant strides in understanding the role of stem cells, dentin growth factors, and biocompatible disinfection in the reestablishment of a vital tissue that fosters continued root development and acceptable clinical outcomes. Further efforts focused on better control of the regenerative process will improve the predictability and acceptance of regenerative endodontic therapies. In conclusion, clinicians must be ready to provide early biocompatible interventions to preserve pulp vitality, accepting their role as "facilitators" of the inherent great regenerative potential of human dental pulp.

Study Questions

5. When the patient presents a dental anomaly such as dens invaginatus or dens evaginatus, the dental pulp can become infected because:
   a. The enamel is less mineralized and prompt to decay.
   b. These patients have higher incidence of cariogenic bacteria.
   c. There is a direct access to bacteria though the malformation.
   d. There is generic predisposition to necrosis.
6. Select the iatrogenic factor that affects the dental pulp.
   a. Coronal leakage from inadequate restorations
   b. The vasoconstriction provoked by dental anesthetics
   c. The lack or cooling while drilling with high-speed burs
   d. All of the above
7. Which of the following is the limitation of regenerative endodontic procedures (REP)?
   a. Resolution of apical periodontitis
   b. Increased stability of the root
   c. Intracanal calcification
   d. Apical closure for immature teeth
8. Which of the following tissue type(s) have been shown to be present in the newly formed tissue after REP?
   a. Bone
   b. Cementum
   c. Fibrous tissues
   d. All of the above
9. Which of the following is NOT a requirement for successful REP?
   a. Bioactive, biocompatible material
   b. Control of inflammation and infection
   c. Presence or recruitment of mesenchymal stem cells
   d. Biomechanical instrumentation of canals

ANSWERS

Answer Box 10

1 e. All of the above
2 c. Pulpectomy
3 a. Use of bioactive dental materials is advocated.
4 a. Anterior maxillary
5 c. There is a direct access to bacteria through the malformation.
6 d. All of the above
7 c. Intracanal calcification
8 d. All of the above
9 d. Biomechanical instrumentation of canals

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