VITAL PULP THERAPY IN PERMANENT TEETH

EDITOR
ASSOC. PROF. NESLİHAN YILMAZ ÇIRAKOĞLU, PH.D.

DOI: 10.5281/zenodo.19226047

Vital Pulp Therapy in Permanent Teeth

Edıtor

Assoc. Prof. Neslihan Yılmaz Çırakoğlu, Ph.D.

Publisher
Platanus Publishing®

Editor in Chief
Assoc. Prof. Neslihan Yılmaz Çırakoğlu, Ph.D.

Cover & Interior Design
Platanus Publishing®

The First Edition
March, 2026

ISBN
978-625-8513-66-9

©copyright
All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, or any information storage or retrieval system, without permission from the publisher.

Platanus Publishing®
Address: Natoyolu Cad. Fahri Korutürk Mah. 157/B, 06480, Mamak, Ankara, Turkey.

Phone: +90 312 390 1 118
web: www.platanuspublishing.com
e-mail: platanuskitap@gmail.com

Platanus Publishing®

CONTENTS

CHAPTER 1 ..... *5*

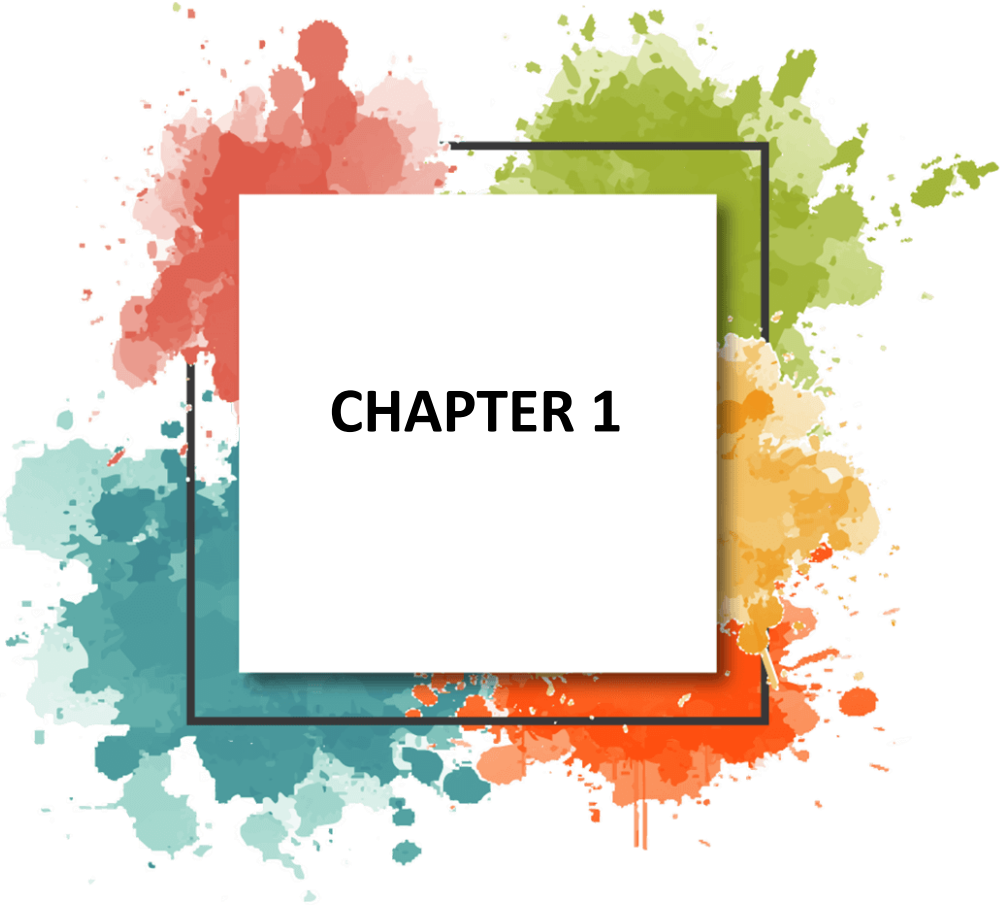
PULP TISSUE: STRUCTURE AND FUNCTION
Sevcan Akça

CHAPTER 2 ..... *35*

INDICATIONS FOR VITAL PULP THERAPY AND THE MATERIALS USED
Duygu Aksoy Çalıoğlu

CHAPTER 3 ..... *53*

PRINCIPLES OF VITAL PULP THERAPY
Gülçin Cagay Sevencan


CHAPTER 1

PULP TISSUE: STRUCTURE AND FUNCTION

Sevcan Akça[1]

Introduction

The dental pulp is a very specialized and vascularized connective tissue that is surrounded by dentin. It serves as a dynamic center that keeps the tooth alive and ensures its proper functioning. This structure comes from the dental papilla during embryonic development. It is very important for both the development of the tooth (dentinogenesis) and keeping the tooth's homeostasis throughout its life cycle. The pulp is a very important part of the "pulp-dentin complex." It is protected by the hard tissues of the tooth and acts as a sensory, nutritive, and most importantly, protective barrier against heat, chemicals, and bacteria from the outside world.

Pulp tissue exhibits a highly organized morphological structure; it consists of an outer layer of odontoblasts, followed by regions with varying degrees of cellular density, and a central pulp core. This layered structure is supported by a rich microvascular network, a complex nervous system, and strategically positioned immune cells. Dental pulp stem cells (DPSCs) located within the pulp have the ability to initiate the repair process (reparative dentinogenesis) by differentiating into odontoblast-like cells when the tissue is damaged. This biological potential demonstrates that the pulp is not merely a sensory tissue but a proactive organ capable of self-protection and regeneration.

In modern endodontics, a deep understanding of pulp biology has become the cornerstone of clinical success. While traditional approaches have primarily focused on the removal of infected tissue, current research aims to preserve pulp vitality and promote regeneration using tissue engineering principles. This section aims to provide a biological foundation for clinical practice by examining the histomorphological structure of dental pulp, its cellular and molecular components, and the complex responses it develops to various pathological conditions, all in light of the current literature.

Keywords: *Dental pulp, dental pulp stem cells (DPSC), dentinogenesis, endodontics, immune response, odontoblasts, pulp-dentin complex, regenerative endodontics*

[1] Assist. Prof. Dr., Department of Endodontics, Faculty of Dentistry, Sakarya University Sakarya, Turkiye, ORCID No: 0000-0002-7544-5325

1. Pulp

Dental pulp tissue is the soft connective tissue inside the tooth that surrounds odontoblasts at the dentin–pulp interface and is enclosed by dentin and, at the crown, by enamel. It comprises a fibrous matrix with a rich network of blood vessels, nerves, resident immune cells, fibroblasts, and dental pulp stem cells (DPSCs) that can differentiate into odontoblast-like cells capable of dentin formation; it also interfaces with dentin via odontoblast processes that extend into dentinal tubules (Tenyi, Milutinović, & Nemeth, 2024; Widbiller & Schmalz, 2020a; Zainuddin, Mohamad, Su Keng, & Mohd Yusof, 2023). The pulp participates in dentinogenesis and reparative dentin formation, mediating responses to caries and injury through signaling pathways (e.g., Wnt, TGF-β, BMP) and regeneration concepts in modern endodontics and tissue engineering (Birjandi & Sharpe, 2021; Moore, Perez, Hartgerink, D'Souza, & Colombo, 2015; Widbiller & Schmalz, 2020a).

1.1. Morphological Layers of Pulp

1.1.1. Odontoblast Layer

The odontoblast layer is defined as the cellular boundary immediately beneath the predentin and consists of odontoblast cell bodies; the extensions of these cells extend into the predentin and dentin (Ohshima, Maeda, & Takano, 1999). Animal experiments have also shown that the odontoblast layer itself consists of cell bodies, but its cytoplasmic extensions extend deeper into the mineralized tissue (Bishop, 1985).

The odontoblast layer contains intercellular and extracellular connections with capillaries, nerves, and dendritic cells. Capillaries are located near the odontoblast layer and predentin, and juxtaodontoblastic capillary plexuses have been identified in developing and mature teeth; their proximity suggests a role in supplying nutrients and transmitting signals at the dentin-pulp border during dentinogenesis (Josephsen, Fejerskov, & Theilade, 1974). Sensory nerve fibers and axons form subodontoblastic plexuses beneath the odontoblast layer and extend into the predentin and dentinal tubules. The density and depth of this innervation vary depending on the region of the tooth (crown vs. root) and the stage of development (Dahl & Mjör, 1973). Dendritic cells and class II MHC-positive cells are found in the odontoblast layer and within the predentin, and their extensions extend toward the dentinal tubules. These cells play regulatory and immunological roles at the dentin-pulp interface, interact with odontoblasts when necessary, and contribute to local immune modulation (Ohshima et al., 1999). The presence of von Korff fibers and other extracellular components

between odontoblasts supports the continuity of dentin-pulp signaling structures throughout the odontoblast layer (Bishop, Malhotra, & Yoshida, 1991).

Odontoblasts actively secreting in young pulp vary in height. Therefore, their nuclei are not at the same level and are typically arranged in a stepped pattern, described as a palisade appearance. This structure is a characteristic feature and allows for the polarized secretion of predentin and dentin matrix components (Bishop et al., 1991). Tight junctions between odontoblast cell bodies and the coexistence of gap junctions at the lateral borders support the barrier properties and intercellular communication necessary for synchronized matrix production and mineralization. The combined actions of the gaps and tight junctions coordinated by connexins support the integrity of dentin formation and the pulp's adaptive response to injury (Muramatsu et al., 2013; Xu et al., 2016).

Mature pulp contains more odontoblasts per unit area in the coronal pulp than in the radicular pulp, consistent with the coronal region being the primary site of dentinogenesis during tooth eruption and having a higher dentin tubule density per unit area. Mature coronal odontoblasts are typically columnar in shape. This structure is consistent with robust dentinogenesis and a high degree of polarization at the coronal dentin-pulp interface. In contrast, odontoblasts in the middle portion tend to be more cuboidal. This structure parallels the regional modulation of the odontoblastic differentiation process and maturation gradient throughout the root region. Odontoblasts near the apical foramen appear as a squamous layer of flattened cells, consistent with the reduced secretory/phenotypic demand in this region and the anatomical tapering of dentin formation near the apex (Shamel, Al Ankily, & Bakr, 2017).

1.1.2. Cell-Poor Zone (Weil Zone)

This area represents a histological region located immediately beneath the odontoblast layer, approximately 40 μm wide, relatively acellular but covered with capillaries, unmyelinated nerve fibers, and fibroblast processes. Its presence varies depending on the functional state of the pulp; it may be more easily detected at certain stages of maturation but may be absent in young pulps with rapid dentin formation or in old pulps undergoing reparative dentinogenesis (Luo et al., 2026). The innervation and vascular structure in the Weil zone support the physiological roles of the pulp, including sensory function and vascular regulation. The Raschkow nerve plexus shapes dentin-pulp signaling during health and disease due to its proximity to odontoblasts (Hossain et al., 2019). In a regenerative context, understanding the Weil zone helps develop strategies to preserve or recreate the natural pulp-dentin architecture, including angiogenesis,

DPSC recruitment, and odontoblastic differentiation, to optimize vital pulp treatments and regenerative endodontic outcomes (Astudillo-Ortiz et al., 2023).

1.1.3. Cell-Rich Zone

The subodontoblastic region of the pulp contains a unique layered structure with a relatively high proportion of fibroblasts compared to the more central pulp. This cell-rich region is particularly prominent in the coronal pulp and decreases toward the radicular pulp (A. Sotirovska Ivkovska, Zabokova-Bilbilova, Georgiev, Bajraktarova Valjakova, & Ivkovski, 2018). In addition to fibroblasts, the cell-rich region may harbor various immune cell populations, including macrophages, dendritic cells, and undifferentiated mesenchymal stem cells (MSCs). The subodontoblastic layer, dominated by fibroblasts, forms part of a supportive stromal niche where extracellular matrix remodeling and paracrine signaling can regulate neighboring odontoblasts and immune cells. Antigen-presenting cells in the dental pulp, particularly MHC class II (HLA-DR)-expressing cells, are frequently found in the subodontoblastic region and near the odontoblast layer, especially in erupting or decayed teeth (Ana Sotirovska Ivkovska, Zabokova-Bilbilova, Georgiev, Bajraktarova Valjakova, & Ivkovski, 2017). Dendritic cells and macrophages in the subodontoblastic region may exhibit various stages of maturation. Dendritic cells (HLA-DR+ or CD68+ subpopulations) can be found in the odontoblast layer/predentin or subodontoblastic region, and some evidence suggests the presence of immature dendritic cells that participate in regulatory interactions with odontoblasts and potentially influence dentinogenesis and reparative responses (J. C. Farges et al., 2003). Mesenchymal stem cells are found within the cell-rich zone and surrounding stroma, contributing to the pulp's regenerative capacity and serving as a reservoir for repair and remodeling (Kok et al., 2022).

1.1.4. Pulp Proper

The central portion of the dental pulp, which is the loose connective tissue core, surrounds the odontoblast layer at the dentin-pulp interface and contains the main blood vessels and nerves that serve the tooth (França et al., 2019). This central mass is distinct from the peripheral subodontoblastic regions and the odontoblast layer itself. Many sources emphasize that the dental pulp consists of a dense vascular and nerve network embedded in loose connective tissue and that the center of the pulp contains a large part of this network (Nosrat, Widenfalk, Olson, & Nosrat, 2001; C. Y. Yu & Abbott, 2018).

1.2. Cells of Pulp Tissue

1.2.1. Odontoblast

The active odontoblast nucleus is typically located at the base of the cell body, is enclosed within a classic nuclear envelope, and may contain a nucleolus. In active odontoblasts, the endoplasmic reticulum (ER) is particularly prominent and consists of tightly stacked cisternae forming parallel arrays widely distributed throughout the cytoplasm. Ribosomes are abundant on the ER membranes, marking the sites where protein synthesis occurs (Couve, 1986). The Golgi apparatus is located in the center of the supranuclear cytoplasm and consists of vesicles associated with Golgi sacs. This organization consistently allows for the processing and packaging of dentin matrix precursors and non-collagenous proteins, as defined in odontoblasts and other collagen-secreting cells, via the canonical ER–Golgi–secretory granule secretory pathway. In odontoblasts, secretory proteins (including dentin matrix proteins, such as dentin phosphoprotein) are synthesized in the ER and accumulate in the Golgi apparatus, from where they are transported via vesicles to odontoblastic processes and predentin/dentin (Weinstock & Leblond, 1974). Along with these, numerous mitochondria are scattered throughout the odontoblast cytoplasm, reflecting the high energy requirements for continuous dentin matrix synthesis and secretion. This distribution is a common feature in secretory cells with strong protein synthesis and secretion activity (Couve, 1986).

Odontoblasts synthesize an extracellular matrix (ECM) that is rich in type I collagen, along with additional non-collagen components that regulate mineralization. In dentin, while a small amount of type V collagen has been reported in the ECM, dentin-specific non-collagen proteins such as dentin sialoprotein (DSP) and dentin phosphoprotein (DPP) are secreted along with proteoglycans (Wallwork et al., 2002). Phosphorin is a highly phosphorylated phosphoprotein that plays a role in extracellular mineralization and is unique to dentin among mesenchymal cell types (Sfeir et al., 2011). Odontoblasts also secrete acid phosphatase and alkaline phosphatase (ALP). Alkaline phosphatase (ALP) activity is closely linked to mineralization. Although the precise mechanistic role of ALP in dentinogenesis is not fully understood, evidence supports a functional relationship with mineral deposition (F. Yu et al., 2016). Acid phosphatase activity, localized in lysosomes, contributes to remodeling events necessary for proper dentin formation by participating in the digestion of resorbed predentin or the remodeling of the predentin matrix (Sasaki et al., 1988).

1.2.2. Pulp Fibroblast

Fibroblasts are the most numerous cells of the pulp. Immature pulp fibroblasts in the dental pulp are characterized by a primitive structure featuring an inconspicuous Golgi apparatus, abundant free ribosomes, and sparse rough endoplasmic reticulum (RER). As maturation progresses, the cells transform into a star shape and acquire the distinct features of protein-secreting cells: an enlarged Golgi apparatus, increased RER, the appearance of secretory vesicles, and active secretory pathways supporting extracellular matrix synthesis. Collagen fibrils then accumulate along the outer surface of the cell body, consistent with active collagen synthesis and secretion. With increased vascularization, innervation, and collagen fiber accumulation, the pulp exhibits a relative decrease in fibroblast density, reflecting the changing cellular demand during maturation and remodeling (Kamakura, 2015).

Given the right signals, these cells can differentiate into odontoblast-like cells. They are responsible for synthesizing and restructuring extracellular matrix (ECM) components, including type I collagen, type III collagen, proteoglycans, and glycosaminoglycans (GAGs) (Dimitrios Tziafas, 2007). The interaction between pulp fibroblasts and their surrounding signaling environment, along with odontoblasts and progenitor cells, affects dentin formation, dentin repair, and the immune response within the pulp. Studies suggest that pulp fibroblasts may be involved in collagen remodeling and transformation, which aligns with the known role of fibroblasts in collagen changes within the pulp (Manríquez-Olmos, Garrocho-Rangel, Pozos-Guillén, Ortiz-Magdaleno, & Escobar-García, 2022).

Odontoblasts and pulp fibroblasts play a role in innate immune responses against bacterial threats. Comparative studies have reported that odontoblast-like cells and pulp fibroblasts generate different innate immune responses to TLR2, TLR3, and TLR4 agonists, exhibit different chemokine expression, and show different innate immune responses by promoting the recruitment of immature dendritic cells (Staquet et al., 2008).

1.2.3. Macrophage

Macrophages in dental pulp constitute a heterogeneous population that plays a central role in tissue homeostasis, defense against bacterial attacks, and regeneration processes. Across species and experimental models, macrophages in dental pulp have been characterized as resident cells exhibiting a phenotypic spectrum most commonly summarized as M1 (proinflammatory) and M2 (anti-inflammatory and repair-supportive). Additionally, intermediate phenotypes are also present. They form a network of immune cells embedded within the central

pulp and along the dentin-pulp boundaries in both developing and mature teeth (Chen et al., 2024; Yoshiba et al., 2020). Macrophages in healthy pulp contribute to surveillance and rapid response to bacterial invasion, phagocytosis, and cytokine production. In inflamed pulp, macrophages contribute to antibacterial defense, secretion of inflammatory mediators (e.g., TNF-α, IL-1β, PGE2), and modulation of the inflammatory environment, thereby contributing to the balance between tissue destruction and repair (Erdogan, Xia, Chiu, & Gibbs, 2023; Watanabe et al., 2020).

1.2.4. Dendritic Cell

Dendritic cells and other class II MHC-expressing immunocompetent cells are abundant in dental pulp and important anatomical interfaces (pulp-dentin junction, predentin, and perivascular regions). In healthy pulp, they are present as dendritic cells and macrophage-like cells and increase or relocate in response to injury or antigenic attack; here they participate in immune surveillance, antigen presentation, and potentially the regulation of odontoblast differentiation and pulp healing. Dendritic cells are usually found near the outer edges, close to the odontoblast layer or predentin, while macrophage-like cells are more centrally located within the pulp core. The ultrastructural features of pulp dendritic cells include tubulovesicular systems and multivesicular bodies, consistent with dendritic cell identity. Some class II MHC-positive cells beneath the odontoblast layer, however, do not possess phagosomes (Nishikawa, 2004; Ohshima et al., 1999).

Following caries preparation, pulp exposure, tooth replantation, laser ablation, or caries attack, class II MHC-positive cells rapidly accumulate or migrate toward the pulp-dentin border or pulp core, depending on the location of the lesion and the time elapsed since the injury. Over time, class II positive cells typically migrate early to the pulp-dentin border within 12–24 hours and then reorganize as regeneration progresses. In addition, studies have shown that pulpal dendritic cells can migrate to regional lymph nodes after capturing antigens, indicating a functional link between pulp immunity and systemic adaptive responses (Nakakura-Ohshima, Watanabe, Kenmotsu, & Ohshima, 2003; Ohshima et al., 2003; Suzuki, Nomura, Maeda, & Ohshima, 2004).

1.2.5. Lymphocyte

Many early immunohistochemical studies have reported the presence of T lymphocytes in normal (non-carious, non-inflamed) dental pulp. Jontell et al. found T lymphocytes in the pulp of teeth showing no signs of decay or periodontal disease and noted that T cells, including helper-inducer and

cytotoxic/suppressor subgroups, were predominant and that B cells were not observed in these samples (Jontell, Gunraj, & Bergenholtz, 1987). In their study presenting an immunohistochemical/morphometric view of dental pulp, Tomaszewska et al. identified memory T cells (CD45RO+) in the pulp and reported that B cells (CD20+) were relatively less frequent. These findings are consistent with a pulp structure rich in T cell-mediated immune components and relatively sparse in B cells in non-inflammatory conditions (Tomaszewska, Miskowiak, Matthews-Brzozowska, & Wierzbicki, 2013).

1.2.6. Mast Cell

Mast cells (MCs) are immune cells containing granules that are widely found in connective tissues, including the oral cavity and dental pulp. MCs are present in dental pulp, but they are often difficult to detect due to degranulation occurring during tissue damage and sampling due to neuropeptide release. Advanced detection techniques, such as immunohistochemical staining for granule proteases and transmission electron microscopy, identify both resident and degranulated mast cells in pulp tissue. Mast cells in dental pulp play a role in initiating and regulating pulp inflammatory responses, modulating vascular responses and endothelial interactions, and neuroimmune cross-talk and nerve-immune network formation (Ghably et al., 2015; Walsh, 2003).

1.3. Innervation of the Pulp

The innervation of the dental pulp primarily originates from sensory neurons located in the trigeminal ganglion, and there are additional autonomic (sympathetic and parasympathetic) fibers accompanying the pulp vascular system. Nerve axons enter the pulp through the apical foramen, ascend into the coronal pulp, and branch extensively to form the subodontoblastic (Raschkow) plexus and terminals in the odontoblast layer and inner dentin. This anatomical arrangement forms the basis for the neural regulation of afferent nociceptive stimuli, pulp blood flow, and local inflammatory responses. Sympathetic and parasympathetic fibers travel alongside blood vessels, contributing to vasoregulation and neurovascular responses during inflammation (Bae & Yoshida, 2020; Ronan, Nagel, & Emrick, 2024; C. Y. Yu & Abbott, 2018).

Different fiber classes and their transmitters produce distinct sensory and regulatory effects in health and disease; they also shape pulp pathology and repair by involving immune and vascular compartments. Aδ afferents, which terminate in the inner dentin and subodontoblastic plexus, are activated by fluid movements in the dentinal tubules (hydrodynamic mechanism) and mediate the characteristic sharp, well-localized dentinal sensitivity and rapid pain. Unmyelinated C fibers

are predominantly polymodal nociceptors that respond to inflammatory mediators and tissue damage, producing the dull, diffuse, and prolonged pain associated with pulpitis (Närhi, 1990). Peptidergic sensory axons release CGRP and substance P, which cause vasodilation, increase vascular permeability, recruit neutrophils/monocytes, and modulate local immune and repair processes; substance P plays an important role in the inflammatory pain of the tooth (Heyeraas, Kvinnsland, Byers, & Jacobsen, 1993). Glutamate released by pulp axons and the expression of vesicular glutamate transporters (VGLUT1/2) and glutamate receptors in axons and trigeminal ganglion neurons contribute to glutamatergic peripheral signaling to the pulp nociceptor and exert a modulatory effect on inflammation (Zhan, Huang, Yang, & Hou, 2021). Transient receptor potential (TRP) channels (e.g., TRPV1) and mechanosensitive channels contribute to pulp nociceptor activation and pro-nociceptive peptide release (Chung, Raman, & Szallasi, 2025).

2. Immune Responses in the Dentin–Pulp Complex

The dentin-pulp complex is organized to reduce microbial threats originating from the oral environment. This defense is based on the peripheral outward flow of dentin fluid through the dentin tubules and the retention of bacteria and bacterial macromolecules on the inner tubule walls. Collectively, these mechanisms reduce the pulp's exposure to harmful substances, thereby providing an effective immune response (Pashley, 1996).

The dental pulp's immunological microenvironment is distinguished by a complex defensive system, encompassing odontoblasts, neurovascular components, and specialized Antigen-Presenting Cells (APCs). Dendritic cells (DCs) and monocyte/macrophage-derived cells, positioned strategically near the dentinal tubules, function as "sentinels" within this network. These cell types both express MHC class II molecules on their surfaces, which are essential for T-lymphocyte activation, facilitating the identification of foreign antigens at both local and regional lymph node sites. In particular, the cytoplasmic contact established between pulp DCs and odontoblasts is the primary mechanism that enables the early diagnosis of microorganisms that have crossed the dentin barrier and the coordination of the systemic immune response (Pohl et al., 2024).

Immature pulp DCs mature after encountering antigens and migrate to regional lymph nodes, where they activate naive T cells, linking the innate response to secondary adaptive immunity. In this process, the macrophage population exhibits significant phenotypic and functional heterogeneity. MHC II-expressing macrophages form a dense immune network together with dendritic

cells, while histiocytes that are concentrated around blood vessels (perivascular) and do not carry MHC II function primarily as resident cells responsible for phagocytosis and tissue debridement. This cellular organization optimizes both antigen presentation and direct cellular defense capacity in the pulp (Quispe-Salcedo & Ohshima, 2021).

Effective repair and regeneration of the dentin-pulp complex enables repair processes while also controlling tissue damage caused by infection and inflammation. This process is evident in the aggregation and differentiation of progenitor cells within the context of low-grade, controlled inflammation. Conversely, the capacity for repair is compromised in the presence of high or chronic inflammation, a consequence of diminished stem cell functionality and impaired tissue regeneration. In the case of rapidly advancing caries, elevated concentrations of proinflammatory cytokines, including TNF-α, and dentin matrix components released by bacterial acids can induce pulp cell death and impede stem cell proliferation and odontoblastic differentiation, thus obstructing repair mechanisms. In contrast, early caries or the resolution of the disease is associated with reduced levels of proinflammatory cytokines, such as IL-1α and IL-1β, which can facilitate repair processes and the differentiation of progenitor cells (Shah et al., 2020).

2.1. Responses of the Healthy Dentin-Pulp Complex to Non-Destructive Stimuli

The dentin-odontoblast unit functions as an alarm system in the peripheral pulp and converts external stimuli into rapid signals capable of initiating a protective retraction response and alerting the organism to potential excessive loads. These stimuli may take the form of thermal stimuli or occlusal forces that do not exceed physiological limits. In response to these non-destructive stimuli, the dentin fluid within the dentin tubules mediates an elastic response to counteract the stimulus (Aminoshariae & Kulild, 2021; Fu & Kim, 2024; Ronan et al., 2024). Activation of nerve endings by these stimuli triggers impulses that spread to the adjacent endings of the same nerve via the axon reflex. Due to the anatomical proximity of nerve fibers to arterioles and capillaries, this stimulation promotes rapid, localized neuropeptide release and vasodilation. CGRP is the primary mediator of this rapid response (Berggreen, Bletsa, & Heyeraas, 2007). This transient increase in local blood volume may elevate tissue pressure; however, within the pulp chamber—which has low compliance—this response is balanced by regulatory vascular mechanisms to prevent ischemia. This compensation is adjusted by the vasodilation of blood vessels in nearby tissues

(known as the “steal” phenomenon) and connections between arteries (Berggreen et al., 2007; C. Y. Yu & Abbott, 2018).

2.2. Responses of the Dentin-Pulp Complex to External Injuries

Constant and repeated irritation of the dentin surface can lead to long-term pulp reactions and trigger a proinflammatory response. Due to the absence of a firm tissue barrier surrounding the pulp tissue and the lack of collateral circulation, the development of inflammatory processes differs from that in other tissues. Severe stimuli result in damage to the integrity of the pulp tissue (C. Yu & Abbott, 2007).

2.2.1. Dental Treatment Procedures

Procedures performed to treat dental pathologies can cause damage to the dentin-pulp complex due to the nature of the procedures. This damage is often preventable and reversible. However, if not reversed, it leads to long-term changes in the pulp (Henry F. Duncan, Kobayashi, Kearney, & Shimizu, 2023). The dentin-pulp complex withstands these factors via reactive dentinogenesis, generated by surviving odontoblasts, and reparative dentinogenesis, produced by odontoblast-like cells originating from pulp progenitors upon the demise of primary odontoblasts (Widbiller & Schmalz, 2020b). The tubular or osteodentin-like matrices that form during reparative dentinogenesis, on the other hand, cause the pulp to become fibrous and mineralized in an irregular way. Parallel to this change, a decrease in the number of pulp cells and disruptions in circulation are observed. These changes also negatively affect the pulp’s immunity against future injuries (Henry F. Duncan et al., 2023; Dimitrios Tziafas & Kodonas, 2015). The current literature lists the primary iatrogenic factors as follows: mechanical exposure or injury during tooth preparation, chemical irritation caused by irrigation fluids, medications, cements, and temporary materials, thermal stimulation resulting from surgical procedures, microleakage and inadequate sealing leading to bacterial entry, and procedural steps during definitive restoration—including impressions and temporary restorations—that compromise dentin thickness and pulp protection.

2.2.1.1. Direct Mechanical Exposure and Dentin/Cavity Preparation

The removal of dentin during crown preparation or other invasive procedures can expose dentin tubules, thereby increasing the pulp’s sensitivity to irritants and inflammatory mediators. If structural integrity is compromised prior to surgery, the risk of pulp exposure and associated pulp pathology is higher (Mohamed Khazin, Abdullah, Liew, Soo, & Ahmad Tarib, 2022).

Treatment of deep caries in teeth with cracks or extensive restorations, as well as during crown preparations, can also lead to iatrogenic pulp damage, particularly when caries-induced demineralization occurs near the pulp or when temporary materials contribute to irritation (Mohamed Khazin et al., 2022).

2.2.1.2. Chemical Irritation

The pulpal tissue is sensitive to chemical irritants, including irrigants such as sodium hypochlorite and other medicaments, as well as luting cements, temporary restorations, impression materials, and other intraoperative substances. Smaller residual dentin thickness magnifies the impact of chemical insults on the pulp under stressed conditions (Abu-Tahun & Torabinejad, 2010; Mohamed Khazin et al., 2022).

Direct pulp capping, pulpotomy materials, and calcium silicate/MTA-based therapeutics reflect ongoing attempts to mitigate chemical irritation and support pulp healing when iatrogenic exposure occurs, highlighting the interaction between material biocompatibility and pulpal outcomes (Abu-Tahun & Torabinejad, 2010; Vaid et al., 2025).

2.2.1.3. Thermal Stimulation During Procedures

Thermal damage from burs, polishing tools, and other equipment is often cited as a potential cause of pulpal inflammation, especially when the pulp is already inflamed or structurally weakened. The main irritants to pulp tissue include thermal stimuli, along with bacterial and chemical factors; their combined effect can lead to pulpal necrosis if not managed. In vitro studies have shown that intrapulpal temperature increases greater than approximately 5.5°C (pulp temperature exceeding about 42.4°C) are associated with detrimental effects including inflammation and necrosis (Lau et al., 2023).

2.2.1.4. Microleakage

A critical iatrogenic risk is microleakage at the restoration margin, which allows bacterial ingress and by-products to irritate the pulp. This issue is particularly relevant in iatrogenic exposures during caries control, pulpotomy, and direct pulp capping, where hemostasis and hermetic sealing are essential for favorable outcomes (H. F. Duncan et al., 2019).

Decisions regarding indirect and direct pulp capping hinge on the preservation of an aseptic operative field and the attainment of a hermetic seal; neglecting these factors may transform reversible pulpitis into irreversible pulpitis or necrosis resulting from ongoing bacterial irritation (H. F. Duncan et al., 2019).

2.2.1.5. Restoration Strategies and Procedural Factors Affecting Pulp Protection

The health of the dental pulp is directly influenced by the success of the final restoration, which includes both the post-core and the crown. To reduce the risk of unintentional pulp damage, a thorough preoperative assessment and careful planning for the restoration are essential. This requires a detailed evaluation of the remaining tooth structure and the use of effective isolation methods (Tait Bds et al., 2005).

For teeth that have undergone root canal treatment or are extensively damaged, restorative interventions necessitate careful consideration of pulp vitality and the risk of leakage, particularly concerning post placement, core design, and crown selection. The integrity of the seal is paramount; therefore, the application of unsuitable techniques or materials can jeopardize it, potentially resulting in pulpal or periapical pathology (Mohamed Khazin et al., 2022).

In vital pulp therapy, the healing process is influenced by factors related to the procedure itself. These include how much decayed dentin is removed, how bleeding is controlled, and the choice of capping material. Although vital pulp therapy is becoming more common, even in cases where the pulp is irreversibly damaged, the success of the treatment depends on the extent of the pulp's exposure and how the resulting wound is managed (Vaid et al., 2025).

3. The Pulp's Response to Enamel-Dentin Lesions

3.1. The Superficial Enamel Lesion and The Early Odontoblast Response

In a cavity that has not reached the enamel-dentin junction, molecular and morphological changes are observed in the pulp and odontoblast layers. The products of demineralization in the enamel and the acidic environment create local chemical stimuli that reach the enamel-dentin junction via the orientation of enamel rods/striae and stimulate the underlying dentin; through these pathways, translucency changes can be observed immediately beneath the dentin. Matrix components and growth factors released from demineralized dentin can activate odontoblasts and pulp cells, thereby increasing the synthesis of collagen and dentin-specific proteins (Bjørndal, Darvann, & Thylstrup, 1998). Furthermore, odontoblast TLRs recognize bacterial products that enter through the cavity, and this TLR-dependent signaling then triggers antimicrobial responses, such as NOS_2/NO, and chemokine production. Both MMPs embedded within the dentin and enzymes from the pulp control the breakdown and remodeling of the matrix,

thereby modulating both progression and repair signals (Kitamura, Kimura, Nakayama, Toyoshima, & Terashita, 2001; Mendes Soares et al., 2021).

In this type of caries, surviving odontoblasts rapidly form reactive dentin by increasing dentin secretion; this is orthodentin accumulated by existing odontoblasts without the need to mobilize new odontoblast-like cells from pulp stem cells. This reaction is part of a continuum ranging from normal dentinogenesis to the formation of adaptive dentin in response to irritation (Goldberg et al., 2008). During this process, there is a morphological reduction in the size of the odontoblast cell body, and a decrease in the cytoplasm-to-nucleus ratio occurs before any evidence of increased dentin mineralization is observed. The cell-rich layer beneath the odontoblasts also becomes less prominent (Couve, 1986).

3.2. Dentin Hypermineralization Prior to Demineralization of Dentin

When an enamel lesion progresses to approximately two-thirds of the enamel thickness, a semi-translucent, hypermineralized dentin region appears immediately beneath the lesion. It has been proposed that intratubular mineralization occurs through a rapid and localized precipitation process in response to demineralization gradients at the enamel-dentin junction. This process is characterized by pH changes at the enamel-dentin interface, as well as the diffusion of minerals, acids, and dissolution products. Subsequently, accumulation may occur through the reprecipitation of dissolved apatite fragments within the tubules and on the tubule walls. This intratubular mineral accumulation, resembling whitlockite, has been described in the literature as a substrate-strengthening event that reduces tubule permeability and may limit bacterial penetration. This phenomenon is clearly associated with an early dentin response preceding bacterial invasion. During this process, the dentin-pulp complex remains viable, and repair mechanisms (odontoblast activity, peritubular/intratubular dentin deposition) can be activated (L Bjørndal, 2002). The literature reports the presence of a semi-translucent or hypermineralized intertubular/intratubular dentin band, accompanied by varying degrees of tubule obstruction depending on the duration and activity of the caries, within or near the carious lesion. In addition to caries-related contexts, similar intratubular mineralization and sclerosis have been reported to develop as a result of the dentin-pulp complex's response during the early stages of caries prior to cavitation and open bacterial invasion of the dentin, as well as in age-related dentin changes (L Bjørndal, 2002; Love & Jenkinson, 2002).

3.3. Dentin Demineralization

Untreated caries spreads from the enamel lesion toward the dentin, extending to and beyond the enamel-dentin junction, and the dentin becomes progressively demineralized prior to cavitation and bacterial infiltration. The contact area between the enamel lesion and the dentin delimits the dentin demineralization zone; thus, the distribution of hypermineralized dentin and demineralized dentin follows the boundaries of the affected enamel lesion and does not extend beyond the boundaries of the associated enamel rods (A. Mazzoni et al., 2015). Demineralization-remineralization cycles are dependent on environmental factors, and once dentin demineralization begins, endogenous proteolytic enzymes released from the dentin catalyze collagen degradation, thereby creating a cyclic process of mineral loss and matrix degradation that depends on local pH, ions, and fluid movement. Endogenous dentin proteases, particularly collagenolytic matrix metalloproteinases (MMPs) and SIBLINGs (Small Integrin-Binding Ligand N-linked Glycoproteins), play a role in the degradation of the dentin matrix when demineralization exposes the organic matrix. MMPs, including MMP-2 and MMP-9 (gelatinases) and possibly MMP-8/MMP-13 (collagenases), are present within the dentin matrix and dentin tubules and are activated under demineralized conditions; this process contributes to collagen degradation, which weakens the dentin structure and adhesive interfaces (A. Mazzoni et al., 2015; Annalisa Mazzoni, Breschi, et al., 2009; Annalisa Mazzoni, Pashley, et al., 2009).

3.4. Tertiary Dentin Formation and the Immune Response to Dentin Caries

Tertiary dentin formation is a coordinated defense mechanism exhibited by the dentin-pulp complex in response to caries or traumatic stimuli. Neural elements (nerve fibers and nociceptors), immune-competent cells (particularly dendritic cells and T-lymphocytes), and odontoblast-derived cells (primary odontoblasts, odontoblast-like cells, and root/progenitor cell niches) (Couve, Osorio, & Schmachtenberg, 2014). The expansion of dendritic cells within the pulp occurs prior to tertiary dentin deposition, and these cells function as the first-line innate immune sensors at the dentin-pulp junction. An increase in the number of T lymphocytes accompanying this cell group is also observed. Matrix-derived osteopontin also plays a significant role in supporting the activity of dendritic cells (Quispe-Salcedo & Ohshima, 2021). An increase in nerve fiber density (including components of the Raschkow plexus) is observed in the region near the odontoblast layer and the predentin-dentin interface. This nerve proliferation facilitates neuroimmune remodeling and increased nociceptive sensitivity during

the early lesion stage. The neural response typically accompanies dendritic cell activity. Studies report simultaneous odontoblast remodeling, increased nerve fiber density, and dendritic cell accumulation as part of a coordinated neuroimmune defense against cariogenic pathogens (Couve et al., 2014; Fristad, Bletsa, & Byers, 2007).

In this process, odontoblasts are not only matrix producers but also active participants in defense signaling. While odontoblasts are involved in recognizing pathogens, secreting antimicrobial factors, and coordinating immune responses, they remain closely connected to nerve endings in the dentinal tubules (Simon, Smith, Lumley, Cooper, & Berdal, 2012; Widbiller & Schmalz, 2020b). Cavity-associated demineralization releases NCPs (non-collagenous proteins) and growth factors (TGF-β1, BMP-7, FGF-2, IGF-1/2, NGF, GDNF) embedded within the dentin, which actively regulate odontoblasts and dentinogenesis (da Rosa, Piva, & da Silva, 2018). Subsequently, primary odontoblasts can form reactive dentin by regulating dentinogenesis. If the injury/caries is severe and odontoblasts are lost, odontoblast-like cells derived from dental pulp stem cells (DPSCs) differentiate to form reparative dentin. The signaling environment governing this transition is provided by growth factors (TGF-β, BMPs, DSPP, DMP-1, and osteopontin) trapped within the dentin matrix and bioactive dentin matrix proteins that are mobilized during demineralization and can direct pulp healing and odontoblast differentiation (Jean Christophe Farges et al., 2015; Dimitrios Tziafas, 2007). The balance between inflammatory and regenerative signals determines whether tertiary dentin formation occurs via a reactive or reparative pathway (Jean Christophe Farges et al., 2015; Simon et al., 2012).

Reactive dentin formation occurs when the remaining odontoblasts become more active, leading to the creation of tubular dentin that has a continuous secondary dentin structure. While the central region near the pulp may still have a higher density of odontoblasts and tubules, the peripheral regions exhibit a more distinct tubular architecture. As odontoblasts form dentin, the predentin matrix expands and forms a characteristic pattern before infection sets in. In reparative dentinogenesis, however, it occurs following the death of odontoblasts and the differentiation of odontoblast-like cells from pulp-derived stem cells (da Rosa et al., 2018; Widbiller & Schmalz, 2020a). Reparative dentin, characterized by a tubular and irregular architecture, often incorporates cellular components. This structural configuration mirrors the participation of root and progenitor cell populations, alongside the intricate cellular arrangement necessary for the closure of the injury site. The morphological characteristics are shaped by the interplay of matrix signals, inflammatory mediators, and neuroimmune signals, which

collectively impact the healing process and the functional recuperation of the tooth's structure (Jean Christophe Farges et al., 2015; Nijakowski, Ortarzewska, Jankowski, Lehmann, & Surdacka, 2023).

4. Pulp Inflammation and Loss of Pulp Vitality

In deep dentin caries, a dense chronic inflammatory cell accumulation occurs in the pulp tissue adjacent to the caries, including macrophages and polymorphonuclear neutrophils (PMNs). The cytokines produced by these cells begin to accumulate in the pulp. Additionally, B lymphocytes accumulate at the periphery of the pulp. At this stage, the bacteria haven't yet reached the pulp, and the inflammation is limited to the coronal pulp. The balance between the damaging and healing aspects of this inflammation will determine the pulp's future health. This balance will decide if the pulp can recover from the initial bacterial invasion or if it will lead to more serious problems like tissue death or permanent damage (Demant, Dabelsteen, & Bjørndal, 2021; H. F. Duncan et al., 2019).

In cases of deep caries that have progressed close to the pulp, the dentin is almost completely demineralized. Cavitation is often present, and tertiary dentin acts as the last barrier against bacteria. When bacteria reach the pulp, the pulp's inflammatory response becomes intense. Because this response usually involves a harmful, destructive inflammatory process, it causes permanent damage to the pulp, such as pulp necrosis and the formation of microabscesses. This damage primarily occurs in the coronal pulp; however, if not treated, it can spread throughout the entire pulp, leading to complete pulp necrosis. As a result, infection from the necrotic tissue within the root canal develops in the later stages after pulp necrosis (Demant et al., 2021; H. F. Duncan et al., 2019; El karim et al., 2021).

Conclusion

The dental pulp is an extremely complex and specialized connective tissue that maintains the vitality and defense mechanisms of the tooth. This organized morphological structure, consisting of the odontoblast layer, regions with varying cell densities, and the pulp core (pulp proper), ensures the coordinated execution of sensory, formative, and immunological functions. The pulp not only plays an active role in the process of dentinogenesis but also develops a continuous surveillance and rapid response mechanism against external stimuli through the strategic distribution of immune cells such as dendritic cells and macrophages. Supported by a rich network of blood vessels and nerves, this biological structure

enables the pulp to function as a dynamic “alarm system” that both transmits nociceptive signals and regulates local physiological processes.

The pulp’s most clinically critical feature is its high adaptability and repair capacity in response to pathological and iatrogenic attacks. Through defense mechanisms such as tertiary dentin formation, the pulp attempts to limit irritants; simultaneously, it produces reparative dentin via surviving odontoblasts or odontoblast-like cells derived from reactive dentin or stem cells. This process is regulated by the complex interaction of neuroimmune signals and bioactive growth factors released from the demineralized dentin matrix. However, the transition from reversible irritation to irreversible necrosis depends on the delicate balance between regenerative pathways and destructive inflammatory responses. This clearly highlights how vital maintaining an aseptic working field and achieving a hermetic seal are for pulp health during restorative procedures.

Endodontic approaches should focus on modulating the pulp microenvironment to support repair rather than destruction, particularly in cases of deep caries or iatrogenic exposure. Understanding the pulp’s innate regenerative potential, stem cell niches, and complex signaling networks forms the cornerstone of regenerative endodontics and tissue engineering applications. Grasping these biological foundations will enable clinicians to pursue vital pulp treatments that preserve the natural tooth structure and long-term function with greater confidence and on a scientific basis.

ABBREVIATIONS

ALP: Alkaline Phosphatase

APCs: Antigen-Presenting Cells

BMP: Bone Morphogenetic Protein

CGRP: Calcitonin Gene-Related Peptide

DCs: Dendritic Cells

DMP-1: Dentin Matrix Acidic Phosphoprotein 1

DPP: Dentin Phosphoprotein

DPSCs: Dental Pulp Stem Cells

DSP: Dentin Sialoprotein

DSPP: Dentin Sialophosphoprotein

ECM: Extracellular Matrix

ER: Endoplasmic Reticulum

FGF-2: Fibroblast Growth Factor 2

GAGs: Glycosaminoglycans

GDNF: Glial Cell Line-Derived Neurotrophic Factor

HLA-DR: Human Leukocyte Antigen – DR isotype

IGF-1/2: Insulin-like Growth Factor 1/2

IL-1α/β: Interleukin-1 alpha/beta

MCs: Mast Cells

MHC: Major Histocompatibility Complex

MMPs: Matrix Metalloproteinases

MSCs: Mesenchymal Stem Cells

MTA: Mineral Trioxide Aggregate

NCPs: Non-Collagenous Proteins

NGF: Nerve Growth Factor

NO: Nitric Oxide

NOS2: Nitric Oxide Synthase 2

PGE2: Prostaglandin E2

PMNs: Polymorphonuclear Neutrophils

RER: Rough Endoplasmic Reticulum

SIBLINGs: Small Integrin-Binding Ligand N-linked Glycoproteins

TGF-β: Transforming Growth Factor beta

TLR: Toll-Like Receptor

TNF-α: Tumor Necrosis Factor alpha

TRP: Transient Receptor Potential

VGLUT1/2: Vesicular Glutamate Transporters 1/2

Wnt: Wingless-related integration site

REFERENCES

Abu-Tahun, I., & Torabinejad, M. (2010). Management of teeth with vital pulps and open apices. *Endodontic Topics*, *23*(1), 79–104. doi:10.1111/j.1601-1546.2012.00287.x

Aminoshariae, A., & Kulild, J. C. (2021). Current Concepts of Dentinal Hypersensitivity. *Journal of Endodontics*, *47*(11), 1696–1702. doi:10.1016/j.joen.2021.07.011

Astudillo-Ortiz, E., Babo, P. S., Sunde, P. T., Galler, K. M., Gomez-Florit, M., & Gomes, M. E. (2023). Endodontic Tissue Regeneration: A Review for Tissue Engineers and Dentists. *Tissue Engineering - Part B: Reviews*, *29*(5), 491–513. doi:10.1089/ten.teb.2022.0211

Bae, Y. C., & Yoshida, A. (2020). Morphological foundations of pain processing in dental pulp. *Journal of Oral Science*, *62*(2), 126–130. doi:10.2334/josnusd.19-0451

Berggreen, E., Bletsa, A., & Heyeraas, K. J. (2007). Circulation in normal and inflamed dental pulp. *Endodontic Topics*, *17*(1), 2–11. doi:10.1111/j.1601-1546.2010.00249.x

Birjandi, A. A., & Sharpe, P. (2021). Wnt Signalling in Regenerative Dentistry. *Frontiers in Dental Medicine*, *2*, 725468. doi:10.3389/fdmed.2021.725468

Bishop, M. A. (1985). Evidence for tight junctions between odontoblasts in the rat incisor. *Cell and Tissue Research*, *239*(1), 137–140. doi:10.1007/BF00214913

Bishop, M. A., Malhotra, M., & Yoshida, S. (1991). Interodontoblastic collagen (von Korff fibers) and circumpulpal dentin formation: An Ultrathin serial section study in the cat. *American Journal of Anatomy*, *191*(1), 67–73. doi:10.1002/aja.1001910107

Bjørndal, L., Darvann, T., & Thylstrup, A. (1998). A Quantitative Light Microscopic Study of the Odontoblast and Subodontoblastic Reactions to Active and Arrested Enamel Caries without Cavitation. *Caries Research*, *32*(1), 59–69. doi:10.1159/000016431

Chen, L., Zhu, M., Zhang, C., Wang, Z., Lyu, X., Xu, W., & Wu, B. (2024). Osteopontin interacts with dendritic cells and macrophages in pulp inflammation: Comprehensive transcriptomic analysis and laboratory investigations. *International Endodontic Journal*, *57*(4), 464–476. doi:10.1111/iej.14028

Chung, M. K., Raman, S., & Szallasi, A. (2025). Tooth Pulp Afferents and Transient Receptor Potential (TRP) Ion Channels as Key Regulators of Pulp

Homeostasis, Inflammation, and Pain. *International Journal of Molecular Sciences 2026, Vol. 27, 27*(1). doi:10.3390/ijms27010182

Couve, E. (1986). Ultrastructural changes during the life cycle of human odontoblasts. *Archives of Oral Biology*, *31*(10), 643–651. doi:10.1016/0003-9969(86)90093-2

Couve, E., Osorio, R., & Schmachtenberg, O. (2014). Reactionary dentinogenesis and neuroimmune response in dental caries. *Journal of Dental Research*, *93*(8), 788–793. doi:10.1177/0022034514539507

da Rosa, W. L. O., Piva, E., & da Silva, A. F. (2018). Disclosing the physiology of pulp tissue for vital pulp therapy. *International Endodontic Journal*, *51*(8), 829–846. doi:10.1111/iej.12906

Dahl, E., & Mjör, I. A. (1973). The structure and distribution of nerves in the pulp-dentin organ. *Acta Odontologica Scandinavica*, *31*(6), 349–356. doi:10.3109/00016357309002522

Demant, S., Dabelsteen, S., & Bjørndal, L. (2021). A macroscopic and histological analysis of radiographically well-defined deep and extremely deep carious lesions: carious lesion characteristics as indicators of the level of bacterial penetration and pulp response. *International Endodontic Journal*, *54*(3), 319–330. doi:10.1111/iej.13424

Duncan, H. F., Galler, K. M., Tomson, P. L., Simon, S., El-Karim, I., Kundzina, R., … Bjørndal, L. (2019). European Society of Endodontology position statement: Management of deep caries and the exposed pulp. *International Endodontic Journal*, *52*(7), 923–934. doi:10.1111/iej.13080

Duncan, Henry F., Kobayashi, Y., Kearney, M., & Shimizu, E. (2023). Epigenetic therapeutics in dental pulp treatment: Hopes, challenges and concerns for the development of next-generation biomaterials. *Bioactive Materials*, *27*(2), 574–593. doi:10.1016/j.bioactmat.2023.04.013

El karim, I. A., Cooper, P. R., About, I., Tomson, P. L., Lundy, F. T., & Duncan, H. F. (2021). Deciphering Reparative Processes in the Inflamed Dental Pulp. *Frontiers in Dental Medicine*, *2*, 651219. doi:10.3389/fdmed.2021.651219

Erdogan, O., Xia, J., Chiu, I. M., & Gibbs, J. L. (2023). Dynamics of Innate Immune Response Due to Bacteria-Induced Pulpitis. *BioRxiv*, 2023.01.15.524125. doi:10.1101/2023.01.15.524125

Farges, J. C., Romeas, A., Melin, M., Pin, J. J., Lebecque, S., Lucchini, M., … Magloire, H. (2003). TGF-β1 induces accumulation of dendritic cells in the odontoblast layer. *Journal of Dental Research*, *82*(8), 652–656. doi:10.1177/154405910308200816

Farges, Jean Christophe, Alliot-Licht, B., Renard, E., Ducret, M., Gaudin, A., Smith, A. J., & Cooper, P. R. (2015). Dental Pulp Defence and Repair Mechanisms in Dental Caries. *Mediators of Inflammation*, *2015*(1), 230251. doi:10.1155/2015/230251

França, C. M., Riggers, R., Muschler, J. L., Widbiller, M., Lococo, P. M., Diogenes, A., & Bertassoni, L. E. (2019). 3D-Imaging of Whole Neuronal and Vascular Networks of the Human Dental Pulp via CLARITY and Light Sheet Microscopy. *Scientific Reports 2019 9:1*, *9*(1), 10860-. doi:10.1038/s41598-019-47221-5

Fristad, I., Bletsa, A., & Byers, M. (2007). Inflammatory nerve responses in the dental pulp. *Endodontic Topics*, *17*(1), 12–41. doi:10.1111/j.1601-1546.2010.00247.x

Fu, X., & Kim, H. S. (2024). Dentin Mechanobiology: Bridging the Gap between Architecture and Function. *International Journal of Molecular Sciences 2024, Vol. 25, 25*(11). doi:10.3390/ijms25115642

Ghably, J., Saleh, H., Vyas, H., Peiris, E., Misra, N., & Krishnaswamy, G. (2015). Paul Ehrlich's Mastzellen: A Historical Perspective of Relevant Developments in Mast Cell Biology. *Methods in Molecular Biology*, *1220*, 3–10. doi:10.1007/978-1-4939-1568-2_1

Goldberg, M., Farges, J. C., Lacerda-Pinheiro, S., Six, N., Jegat, N., Decup, F., … Poliard, A. (2008). Inflammatory and immunological aspects of dental pulp repair. *Pharmacological Research*, *58*(2), 137–147. doi:10.1016/j.phrs.2008.05.013

Heyeraas, K. J., Kvinnsland, I., Byers, M. R., & Jacobsen, E. B. (1993). Nerve fibers immunoreactive to protein gene product 9.5, calcitonin gene-related peptide, substance p, and neuropeptide y in the dental pulp, periodontal ligament, and gingiva in cats. *Acta Odontologica Scandinavica*, *51*(4), 207–221. doi:10.3109/00016359309040569

Hossain, M. Z., Bakri, M. M., Yahya, F., Ando, H., Unno, S., & Kitagawa, J. (2019). The Role of Transient Receptor Potential (TRP) Channels in the Transduction of Dental Pain. *International Journal of Molecular Sciences 2019, Vol. 20, 20*(3). doi:10.3390/ijms20030526

Jontell, M., Gunraj, M. N., & Bergenholtz, G. (1987). Immunocompetent Cells in the Normal Dental Pulp. *Journal of Dental Research*, *66*(6), 1149–1153. doi:10.1177/00220345870660061101

Josephsen, K., Fejerskov, O., & Theilade, J. (1974). Age changes in juxtaodontoblastic capillaries of rat molars. *European Journal of Oral Sciences*, *82*(8), 574–578. doi:10.1111/j.1600-0722.1974.tb01911.x

Kamakura, S. (2015). Tooth and Tooth-Supporting Structures. *Springer Series in Biomaterials Science and Engineering*, *3*, 99–122. doi:10.1007/978-3-662-46836-4_5

Kitamura, C., Kimura, K., Nakayama, T., Toyoshima, K., & Terashita, M. (2001). Primary and secondary induction of apoptosis in odontoblasts after cavity preparation of rat molars. *Journal of Dental Research*, *80*(6), 1530–1534. doi:10.1177/00220345010800061001

Kok, Z. Y., Alaidaroos, N. Y. A., Alraies, A., Colombo, J. S., Davies, L. C., Waddington, R. J., … Moseley, R. (2022). Dental Pulp Stem Cell Heterogeneity: Finding Superior Quality "Needles" in a Dental Pulpal "Haystack" for Regenerative Medicine-Based Applications. *Stem Cells International*, *2022*(1), 9127074. doi:10.1155/2022/9127074

L Bjørndal. (2002). Dentin and pulp reactions to caries and operative treatment: biological variables affecting treatment outcome. *Endodontic Topics*, *2*(1), 10–23. doi:10.1034/j.1601-1546.2002.20102.x

Lau, X. E., Liu, X., Chua, H., Wang, W. J., Dias, M., & Choi, J. J. E. (2023). Heat generated during dental treatments affecting intrapulpal temperature: a review. *Clinical Oral Investigations 2023 27:5*, *27*(5), 2277–2297. doi:10.1007/s00784-023-04951-1

Love, R. M., & Jenkinson, H. F. (2002). Invasion of dentinal tubules by oral bacteria. *Critical Reviews in Oral Biology and Medicine*, *13*(2), 171–183. doi:10.1177/154411130201300207

Luo, W., Yang, M., Zhan, C., Shen, Z., Song, Z., Lin, Z., & Chen, L. (2026). Unveiling the Vital Role of Dental Nerves in Dental Pulp Immune Defence and Repair. *International Endodontic Journal*, *59*(1), 2–18. doi:10.1111/iej.70040

Manríquez-Olmos, L., Garrocho-Rangel, A., Pozos-Guillén, A., Ortiz-Magdaleno, M., & Escobar-García, D. M. (2022). Effect of tricalcium silicate cements in gene expression of COL1A1, MAPK's, and NF-κB, and cell adhesion in primary teeth' pulp fibroblasts. *Journal of Clinical Pediatric Dentistry*, *46*(6), 17–24. doi:10.22514/jocpd.2022.021

Mazzoni, A., Tjäderhane, L., Checchi, V., Di Lenarda, R., Salo, T., Tay, F. R., … Breschi, L. (2015). Role of dentin MMPs in caries progression and bond stability. *Journal of Dental Research*, *94*(2), 241–251. doi:10.1177/0022034514562833

Mazzoni, Annalisa, Breschi, L., Carrilho, M., Nascimento, F. D., Orsini, G., Ruggeri, A., … Tjäderhane, L. (2009). A review of the nature, role, and function of dentin non-collagenous proteins. Part II: enzymes, serum proteins, and

growth factors. *Endodontic Topics*, *21*(1), 19–40. doi:10.1111/j.1601-1546.2012.00268.x

Mazzoni, Annalisa, Pashley, D. H., Tay, F. R., Gobbi, P., Orsini, G., Ruggeri, A., … Breschi, L. (2009). Immunohistochemical identification of MMP-2 and MMP-9 in human dentin: Correlative FEI-SEM/TEM analysis. *Journal of Biomedical Materials Research Part A*, *88A*(3), 697–703. doi:10.1002/jbm.a.31920

Mendes Soares, I. P., Anovazzi, G., Anselmi, C., Leite, M. L., Scheffel, D. L. S., Soares, D. G., … Hebling, J. (2021). Response of pulp cells to resin infiltration of enamel white spot-like lesions. *Dental Materials*, *37*(6), e329–e340. doi:10.1016/j.dental.2021.01.014

Mohamed Khazin, S., Abdullah, D., Liew, A. K. C., Soo, E., & Ahmad Tarib, N. (2022). Pulpal and periapical disease in crowned vital teeth: A prospective matched cohort study. *Australian Endodontic Journal*, *48*(1), 8–19. doi:10.1111/aej.12567

Moore, A. N., Perez, S. C., Hartgerink, J. D., D'Souza, R. N., & Colombo, J. S. (2015). Ex vivo modeling of multidomain peptide hydrogels with intact dental pulp. *Journal of Dental Research*, *94*(12), 1773–1781. doi:10.1177/0022034515600380

Muramatsu, T., Hashimoto, S., Shibukawa, Y., Yuasa, K., Furusawa, M., & Shimono, M. (2013). Immunoelectron microscopic observation of connexin43 in rat odontoblasts. *Microscopy Research and Technique*, *76*(10), 988–991. doi:10.1002/jemt.22271

Nakakura-Ohshima, K., Watanabe, J. I., Kenmotsu, S. I., & Ohshima, H. (2003). Possible role of immunocompetent cells and the expression of heat shock protein-25 in the process of pulpal regeneration after tooth injury in rat molars. *Journal of Electron Microscopy*, *52*(6), 581–591. doi:10.1093/jmicro/52.6.581

Närhi, M. V. O. (1990). Intradental sensory units. *Dynamic Aspects of Dental Pulp*, 137–149. doi:10.1007/978-94-009-0421-7_8

Nijakowski, K., Ortarzewska, M., Jankowski, J., Lehmann, A., & Surdacka, A. (2023). The Role of Cellular Metabolism in Maintaining the Function of the Dentine-Pulp Complex: A Narrative Review. *Metabolites 2023, Vol. 13, 13*(4). doi:10.3390/metabo13040520

Nishikawa, S. (2004). Cystatin C-positive Macrophages and Dendritic Cells in the Rat Incisor Pulp. *ACTA HISTOCHEMICA ET CYTOCHEMICA*, *37*(5), 313–318. doi:10.1267/ahc.37.313

Nosrat, I. V., Widenfalk, J., Olson, L., & Nosrat, C. A. (2001). Dental Pulp Cells Produce Neurotrophic Factors, Interact with Trigeminal Neurons in Vitro, and Rescue Motoneurons after Spinal Cord Injury. *Developmental Biology*, *238*(1), 120–132. doi:10.1006/dbio.2001.0400

Ohshima, H., Maeda, T., & Takano, Y. (1999). The distribution and ultrastructure of class II MHC-positive cells in human dental pulp. *Cell and Tissue Research*, *295*(1), 151–158. doi:10.1007/s004410051221

Ohshima, H., Nakakura-Ohshima, K., Takeuchi, K., Hoshino, M., Takano, Y., & Maeda, T. (2003). Pulpal regeneration after cavity preparation, with special reference to close spatio-relationships between odontoblasts and immunocompetent cells. *Microscopy Research and Technique*, *60*(5), 483–490. doi:10.1002/jemt.10289

Pashley, D. H. (1996). Dynamics of the pulpo-dentin complex. *Critical Reviews in Oral Biology and Medicine*, *7*(2), 104–133. doi:10.1177/10454411960070020101

Pohl, S., Akamp, T., Smeda, M., Uderhardt, S., Besold, D., Krastl, G., … Widbiller, M. (2024). Understanding dental pulp inflammation: from signaling to structure. *Frontiers in Immunology*, *15*, 1474466. doi:10.3389/fimmu.2024.1474466

Quispe-Salcedo, A., & Ohshima, H. (2021). The Role of Dendritic Cells during Physiological and Pathological Dentinogenesis. *Journal of Clinical Medicine 2021, Vol. 10, 10*(15). doi:10.3390/jcm10153348

Ronan, E. A., Nagel, M., & Emrick, J. J. (2024). The anatomy, neurophysiology, and cellular mechanisms of intradental sensation. *Frontiers in Pain Research*, *5*, 1376564. doi:10.3389/fpain.2024.1376564

Sasaki, T., Motegi, N., Suzuki, H., Watanabe, C., Tadokoro, K., Yanagisawa, T., & Higashi, S. (1988). Dentin resorption mediated by odontoclasts in physiological root resorption of human deciduous teeth. *American Journal of Anatomy*, *183*(4), 303–315. doi:10.1002/aja.1001830404

Sfeir, C., Lee, D., Li, J., Zhang, X., Boskey, A. L., & Kumta, P. N. (2011). Expression of phosphophoryn is sufficient for the induction of matrix mineralization by mammalian cells. *Journal of Biological Chemistry*, *286*(23), 20228–20238. doi:10.1074/jbc.M110.209528

Shah, D., Lynd, T., Ho, D., Chen, J., Vines, J., Jung, H. D., … Cheon, K. (2020). Pulp–Dentin Tissue Healing Response: A Discussion of Current Biomedical Approaches. *Journal of Clinical Medicine 2020, Vol. 9, 9*(2). doi:10.3390/jcm9020434

Shamel, M., Al Ankily, M. M., & Bakr, M. (2017). Proliferative Capacity and Differentiation Potential of Isolated Postnatal Human Dental Pulp Stem Cells in Diabetic Patients. *Journal of Stem Cell Research*. doi:10.33140/SCRI

Simon, S., Smith, A. J., Lumley, P. J., Cooper, P. R., & Berdal, A. (2012). The pulp healing process: from generation to regeneration. *Endodontic Topics*, *26*(1), 41–56. doi:10.1111/etp.12019

Sotirovska Ivkovska, A., Zabokova-Bilbilova, E., Georgiev, Z., Bajraktarova Valjakova, E., & Ivkovski, L. (2018). Immunohistochemical study on antigen-presenting cells in healthy and carious human teeth. *Bratislavske Lekarske Listy*, *119*(4), 249–253. doi:10.4149/BLL_2018_047

Sotirovska Ivkovska, Ana, Zabokova-Bilbilova, E., Georgiev, Z., Bajraktarova Valjakova, E., & Ivkovski, L. (2017). Innate immune response of the dental pulp in healthy and carious human teeth. *Macedonian Pharmaceutical Bulletin*, *63*(01), 41–46. doi:10.33320/maced.pharm.bull.2017.63.01.004

Staquet, M. J., Durand, S. H., Colomb, E., Ŕoméas, A., Vincent, C., Bleicher, F., … Farges, J. C. (2008). Different roles of odontoblasts and fibroblasts in immunity. *Journal of Dental Research*, *87*(3), 256–261. doi:10.1177/154405910808700304

Suzuki, T., Nomura, S., Maeda, T., & Ohshima, H. (2004). An immunocytochemical study of pulpal responses to cavity preparation by laser ablation in rat molars by using antibodies to heat shock protein (Hsp) 25 and class II MHC antigen. *Cell and Tissue Research 2004 315:3*, *315*(3), 311–319. doi:10.1007/s00441-003-0840-z

Tait Bds, C. M. E., Mrd, R. E., Eng, R., Ricketts Bds, D. N. J., Rcs, F., Dent, R., & Bds, A. J. H. (2005). Restoration of the root-filled tooth: pre-operative assessment. *British Dental Journal 2005 198:7*, *198*(7), 395–404. doi:10.1038/sj.bdj.4812187

Tenyi, A., Milutinović, A., & Nemeth, L. (2024). Expression of CD31, CD34, and smooth muscle actin (SMA) in endothelial cells of dental pulp vessels. *Pmc.Ncbi.Nlm.Nih.GovA Tenyi, A Milutinović, L NemethBiomolecules and Biomedicine, 2024•pmc.Ncbi.Nlm.Nih.Gov*, *24*(4), 821–826. doi:10.17305/bb.2023.9988

Tomaszewska, J. M., Miskowiak, B., Matthews-Brzozowska, T., & Wierzbicki, P. (2013). Characteristics of dental pulp in human upper first premolar teeth based on immunohistochemical and morphometric examinations. *Folia Histochemica et Cytobiologica*, *51*(2), 149–155. doi:10.5603/FHC.2013.0023

Tziafas, Dimitrios. (2007). Dentinogenic potential of the dental pulp: facts and hypotheses. *Endodontic Topics*, *17*(1), 42–64. doi:10.1111/j.1601-1546.2010.00248.x

Tziafas, Dimitrios, & Kodonas, K. (2015). Dentinogenic Specificity in the Preclinical Evaluation of Vital Pulp Treatment Strategies: A Critical Review. *Dentistry Journal 2015, Vol. 3, Pages 133-156*, *3*(4), 133–156. doi:10.3390/dj3040133

Vaid, S., Ade, A., Mishra, A., Paul, B., Dube, K., Singh, R., … Ghosh, M. (2025). Assessment of biodentine, mineral trioxide aggregate and enamel matrix derivative as direct pulp-capping agents. *Bioinformation*, *21*(8), 2675. doi:10.6026/973206300212675

Wallwork, M. L., Kirkham, J., Chen, H., Chang, S. X., Robinson, C., Smith, D. A., & Clarkson, B. H. (2002). Binding of dentin noncollagenous matrix proteins to biological mineral crystals: An atomic force microscopy study. *Calcified Tissue International*, *71*(3), 249–255. doi:10.1007/s00223-001-1011-4

Walsh, L. J. (2003). Mast cells and oral inflammation. *Critical Reviews in Oral Biology and Medicine*, *14*(3), 188–198. doi:10.1177/154411130301400304

Watanabe, T., Kamio, N., Okabe, T., Hayama, T., Fukai, J., Watanabe, A., … Matsushima, K. (2020). Macrophage Migration Inhibitory Factor Promotes Inflammation in Human Dental Pulp. *Journal of Hard Tissue Biology*, *29*(1), 9–16. doi:10.2485/jhtb.29.9

Weinstock, M., & Leblond, C. P. (1974). SYNTHESIS, MIGRATION, AND RELEASE OF PRECURSOR COLLAGEN BY ODONTOBLASTS AS VISUALIZED BY RADIOAUTOGRAPHY AFTER [3H]PROLINE ADMINISTRATION. *Journal of Cell Biology*, *60*(1), 92–127. doi:10.1083/jcb.60.1.92

Widbiller, M., & Schmalz, G. (2020a). Endodontic regeneration: hard shell, soft core. *Odontology 2020 109:2*, *109*(2), 303–312. doi:10.1007/s10266-020-00573-1

Widbiller, M., & Schmalz, G. (2020b). Endodontic regeneration: hard shell, soft core. *Odontology 2020 109:2*, *109*(2), 303–312. doi:10.1007/s10266-020-00573-1

Xu, J., Shao, M., Pan, H., Wang, H., Cheng, L., Yang, H., & Hu, T. (2016). Novel role of zonula occludens-1: A tight junction protein closely associated with the odontoblast differentiation of human dental pulp cells. *Cell Biology International*, *40*(7), 787–795. doi:10.1002/cbin.10617

Yoshiba, N., Edanami, N., Ohkura, N., Maekawa, T., Takahashi, N., Tohma, A., … Yoshiba, K. (2020). M2 Phenotype Macrophages Colocalize with Schwann

Cells in Human Dental Pulp. *Journal of Dental Research*, *99*(3), 329–338. doi:10.1177/0022034519894957

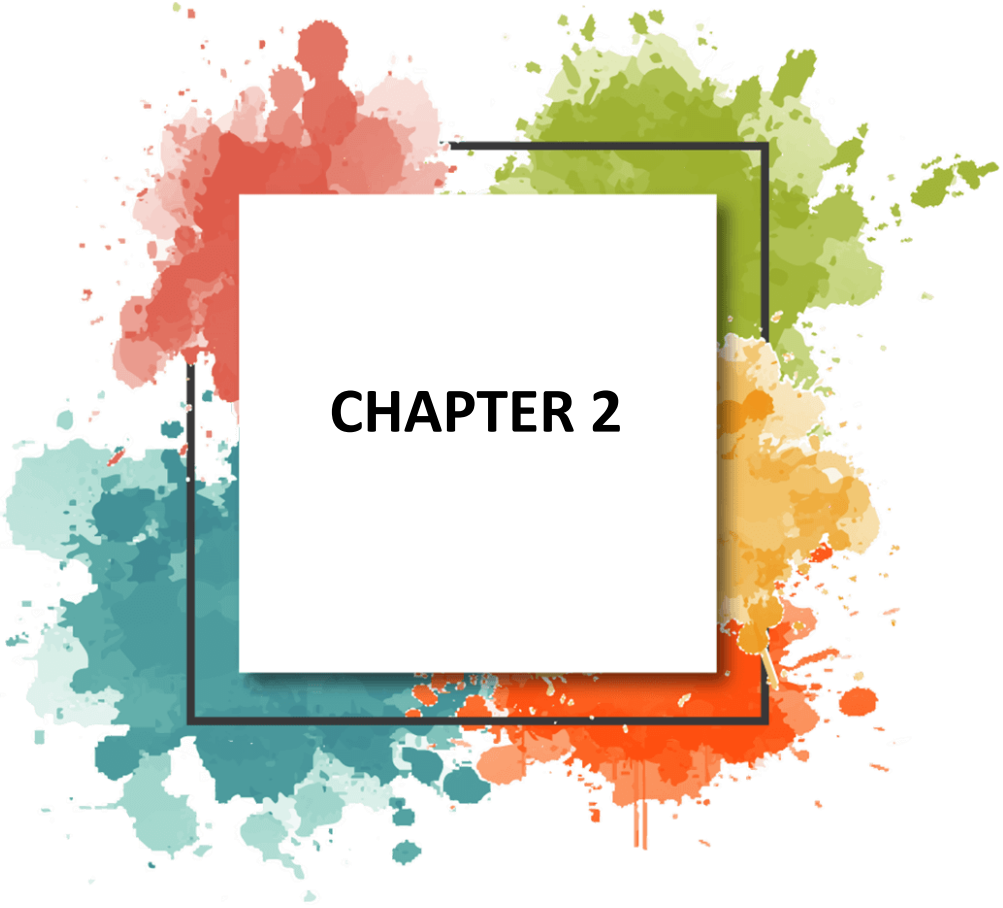
Yu, C., & Abbott, P. V. (2007). An overview of the dental pulp: Its functions and responses to injury. *Australian Dental Journal*, *52*(1 SUPPL.), S4–S6. doi:10.1111/j.1834-7819.2007.tb00525.x

Yu, C. Y., & Abbott, P. V. (2018). Pulp microenvironment and mechanisms of pain arising from the dental pulp - from an endodontic perspective. *Australian Endodontic Journal*, *44*(2), 82–98. doi:10.1111/aej.12257

Yu, F., Dong, Y., Yang, Y. W., Lin, P. T., Yu, H. H., Sun, X., … Chen, J. H. (2016). Effect of an Experimental Direct Pulp-capping Material on the Properties and Osteogenic Differentiation of Human Dental Pulp Stem Cells. *Scientific Reports 2016 6:1*, *6*(1), 34713-. doi:10.1038/srep34713

Zainuddin, M. Z., Mohamad, N. S., Su Keng, T., & Mohd Yusof, M. Y. P. (2023). The applications of MicroCT in studying age-related tooth morphological change and dental age estimation: A scoping review. *Journal of Forensic Sciences*, *68*(6), 2048–2056. doi:10.1111/1556-4029.15352

Zhan, C., Huang, M., Yang, X., & Hou, J. (2021). Dental nerves: a neglected mediator of pulpitis. *International Endodontic Journal*, *54*(1), 85–99. doi:10.1111/iej.13400


CHAPTER 2

INDICATIONS FOR VITAL PULP THERAPY AND THE MATERIALS USED

Duygu Aksoy Çalıoğlu[1]

1. Indications for Vital Pulp Therapy

Vital pulp therapies (VPT) are biological treatment approaches aimed at preserving the vitality of the dental pulp and are particularly indicated in cases where reversible pulpal inflammation is present. The primary objectives of these therapies are to maintain the functional integrity of the pulp tissue, sustain the process of dentinogenesis, and support apexogenesis in teeth with incomplete root development (Marques, Wesselink, & Shemesh, 2015). Over the years, endodontic treatment methods have more and more shifted toward minimally invasive approaches aimed at preserving the biological integrity of the dentin–pulp complex. Within this framework, vital pulp therapy has emerged as a biologically driven alternative to conventional root canal treatment in teeth with deep caries and a vital pulp diagnosis (Duncan, Tomson, Simon, & Bjørndal, 2021). With the advancement of bioceramic materials and an improved understanding of pulpal healing mechanisms, the indications for vital pulp therapies have expanded considerably in recent years (Camilleri, 2015).

Vital pulp treatments can be applied to both primary and permanent teeth. Although young permanent teeth have particular importance for the preservation of pulp vitality. Maintaining pulp vitality enables the continuation of the tooth's proprioceptive function and supports ongoing dentin formation. Furthermore, preservation of the pulp may eliminate the need for root canal treatment and contribute to an improved long-term prognosis of the tooth (Aguilar & Linsuwanont, 2011; Duncan, 2022).

Clinical and radiographic findings are both important for vital pulp therapy indications. The most common indications are listed below:

[1] Assist. Prof. Dr., Department of Endodontics, Faculty of Dentistry, Zonguldak Bülent Ecevit University, Zonguldak, Turkey, ORCID No: 0000-0002-9987-6381

1.1. Deep Dentin Caries

Vital pulp therapy may be indicated in cases of deep dentin caries when the pulp has not yet undergone irreversible inflammation. In situations like this, the main approach is the removal of carious dentin while preserving the vitality of the pulp tissue. Indirect pulp capping is particularly preferred in these situations, as it aims to prevent pulp exposure and promote pulpal healing (Barrett & O'Sullivan, 2021; Bjørndal, Simon, Tomson, & Duncan, 2019).

1.2. Mechanical pulp exposures

Mechanical pulp exposures that occur during restorative procedures or as a result of trauma an important indication for vital pulp therapy. In such cases, the success of the treatment largely depends on the health status of the pulp tissue and the presence of minimal bacterial contamination (Emara, Krois, & Schwendicke, 2020).

1.3. Traumatic pulp exposures

In cases of pulp exposure resulting from trauma, direct pulp capping or partial pulpotomy may be performed when the pulp tissue remains vital. In young permanent teeth, partial pulpotomy has been shown high success rates. (Witherspoon, 2008).

1.4. Reversible pulpitis

Vital pulp therapy may be performed in teeth presenting clinical signs of reversible pulpitis. In situations like this, spontaneous pain is characteristically absent, and experience of pain is generally short-lasting and stimulus-related. Additionally, percussion sensitivity and radiographic evidence of periapical pathology are generally not observed (Sachdeva et al., 2025).

1.5. Teeth with incomplete root development

In young permanent teeth with open apices, preservation of pulp vitality is critical for the continuation of root development. Therefore, vital pulp therapy represents a more conservative and biologically based approach compared with root canal treatment in these teeth (Kandemir Demirci, Kaval, Güneri, & Çalışkan, 2020).

1.6. Clinical confirmation of pulp vitality

In order to perform vital pulp therapy, the vitality of the pulp must be clinically confirmed. This condition is generally evaluated according to the following criteria (Raoof et al., 2022):

- Positive pulp vitality tests
- Absence of spontaneous pain or presence of only short-lasting pain
- Absence of percussion sensitivity
- No radiographic evidence of periapical pathology

In addition, the ability to control bleeding following pulp exposure is considered an important indicator of pulp health (Gomez-Sosa et al., 2024).

When appropriate case selection is combined with the use of biocompatible materials, vital pulp therapies can achieve high success rates. Therefore, approaches aimed at preserving pulp vitality have gained increasing importance in modern endodontic practice (Ramani et al., 2022).

2. Procedures That Induce Mineralized Tissue Barrier Formation

Vital pulp therapy involves biological treatment approaches aimed at preserving pulp vitality and promoting the healing of the pulp tissue. Essentially, the goal of vital pulp treatments is to preserve the integrity of the pulp tissue and facilitate the formation of a protective mineralized tissue barrier on the pulp. Biologically, the success of vital pulp therapy relies on the intrinsic reparative capacity of the dentin–pulp complex. Gentle stimuli stimulate surviving odontoblasts to produce reactionary dentin, whereas more severe injury leading to odontoblast loss activates dental pulp stem cells, which differentiate into odontoblast-like cells and produce reparative tertiary dentin (Aguilar & Linsuwanont, 2011). When appropriate case selection, effective infection control, and the use of biocompatible materials are ensured, the pulp tissue possesses the potential for healing and the formation of reparative dentin may occur (Bjørndal et al., 2019). To summarize briefly, the success of pulpal healing relies on several essential factors, including favorable biological conditions, effective control of bacterial infection, and the use of bioactive materials capable of stimulating stem cell recruitment and subsequent differentiation (Duncan et al., 2021).

Vital pulp therapy procedures are classified as indirect pulp capping, direct pulp capping, partial pulpotomy, and full pulpotomy. All of these aimed at inducing the formation of a mineralized tissue barrier. These procedures differ according to the extent of pulp tissue removal. However, the primary objective of all these approaches is to preserve pulp vitality and promote the formation of a protective hard tissue barrier over the pulp (Berman & Hargreaves, 2020).

2.1. Indirect Pulp Capping

Indirect pulp capping is a conservative treatment procedure applied in cases where the pulp has not yet been exposed but there is a risk of pulp exposure due to deep caries. With this method, pulp tissue is preserved, bacterial contamination is reduced, and the formation of tertiary dentin is stimulated.

While applying an indirect pulp capping to a tooth, infected dentin is removed and a portion of the affected dentin near the pulp is preserved. Thus, pulp exposure is avoided and a favorable environment is created for the healing of the pulp–dentin complex. After that, a biocompatible material is placed over the remaining dentin, and the cavity is restored to ensure an adequate seal (Warreth, 2023).

Clinical studies have demonstrated that indirect pulp capping exhibits high success rates when appropriate case selection and adequate coronal sealing are achieved (Schwendicke & Göstemeyer, 2016).

2.2. Direct Pulp Capping

Direct pulp capping is a treatment procedure performed when the pulp tissue becomes exposed due to mechanical, traumatic, or caries-related causes. In direct pulp capping, a biocompatible material is placed directly over the exposed pulp. Thus, pulp vitality is preserved and formation of a dentin bridge is promoted.

Several factors are important for the success of direct pulp capping, these are pulpal inflammation, effective control of bleeding, and the biocompatibility of the material used (Mente et al., 2010). Using of calcium silicate–based materials such as mineral trioxide aggregate (MTA) and Biodentine has resulted in higher success rates compared with traditional calcium hydroxide materials. (Camilleri, 2015).

2.3. Partial Pulpotomy

Partial pulpotomy is a treatment procedure based on the removal of a limited portion of inflamed pulp tissue located directly beneath the site of pulp exposure. In partial pulpotomy, the superficially inflamed pulp tissue is removed. Thus, underlying healthy pulp tissue is preserved.

Partial pulpotomy is particularly recommended in cases of traumatic pulp exposure and in young permanent teeth with incomplete root development. Since this method preserves a large portion of the pulp tissue, it allows the continuation of root development (Donnelly, Foschi, McCabe, & Duncan, 2022).

The literature has reported that partial pulpotomy demonstrates high clinical success rates and supports pulp healing.

2.4. Full Pulpotomy

Full pulpotomy is a vital pulp therapy procedure based on the complete removal of the coronal pulp tissue while preserving the vitality of the radicular pulp. In this procedure, after the coronal pulp is removed, a biocompatible material is applied over the remaining radicular pulp tissue with the aim of promoting pulp healing and the formation of a mineralized tissue barrier (Louzada, Hildebrand, Neuhaus, & Duncan, 2025).

Traditionally, full pulpotomy has been performed primarily in primary teeth; however, recent studies have demonstrated that with the use of calcium silicate–based bioceramic materials, this procedure can also yield successful outcomes in permanent teeth (Taha & Albakri, 2024). These developments have increased the importance of full pulpotomy in modern endodontic treatment approaches.

3. Materials Used in Vital Pulp Therapy

The success of vital pulp therapy largely depends on the biological properties of the material used. Materials used in vital pulp treatment must have certain characteristics. These materials should be biocompatible, possess antibacterial properties, maintain minimal inflammation in the pulp tissue, and promote the formation of reparative dentin. Also seal effectiveness is expected for preventing bacterial microleakage and supportting the healing of the pulp tissue. (Berman & Hargreaves, 2020; Sachdeva et al., 2025).

Calcium hydroxide has retained its popularity in vital pulp treatment for many years but, in recent years, calcium silicate–based bioceramic materials have increasingly been preferred due to their superior biological and physical properties. These materials promote biomineralization in the pulp tissue, contributing to the formation of a more homogeneous and stable dentin bridge. (Parirokh, Torabinejad, & Dummer, 2018).

The main materials used in vital pulp therapy are summarized below.

3.1. Calcium Hydroxide

Calcium hydroxide has long been considered the gold standard material in vital pulp therapy. This material possesses a highly alkaline pH (approximately pH 12), which provides antibacterial properties. In addition, it stimulates mineralization within the pulp tissue and promotes the formation of a dentin bridge (Emara et al., 2020).

However, it has been reported that the dentin bridge formed with calcium hydroxide is often porous in structure and may undergo dissolution over time. In addition, the material's low mechanical strength and limited resistance to microleakage may negatively affect its clinical success. (Mente et al., 2010).

Due to these disadvantages, calcium hydroxide has largely been replaced in recent years by calcium silicate–based bioceramic materials.

3.2. Conventional Calcium Silicate–Based Bioceramic Materials (NRM-CSMs)

In recent years, calcium silicate–based bioceramic materials have gained an important role in vital pulp therapy. These materials promote biomineralization in the pulp tissue and support the formation of a dentin bridge.

The main properties of these materials include:

- High biocompatibility
- Antibacterial effects
- Good marginal sealing ability
- Promotion of hydroxyapatite formation
- Support of pulp healing

Materials in this group include **MTA**(Mineral Trioxide Aggregate), **Biodentine**, **CEM, EndoSequence BC RRM, iRoot BP Plus, BioRoot RCS,** and other bioceramic-based materials. (Camilleri, 2022).

The development of these materials has significantly contributed to the improvement of success rates in vital pulp therapies and has enabled biologically based approaches aimed at preserving pulp vitality to gain greater prominence in modern endodontics.

3.2.1. Mineral Trioxide Aggregate (MTA)

Mineral trioxide aggregate (MTA) is one of the most commonly used bioceramic materials in vital pulp therapy. MTA is composed of components such as tricalcium silicate, dicalcium silicate, tricalcium aluminate, and bismuth oxide.

MTA is a material that exhibits high biocompatibility and a low inflammatory response in the pulp tissue. Due to its hydrophilic nature, it is capable of setting in a moist environment and provides an effective marginal seal. Thus pulp capping and pulpotomy procedures demonsrate high success with MTA. (Cervino et al., 2020).

MTA also promotes the formation of hydroxyapatite and supports the development of a dentin bridge over the pulp which is high qualified. But it has long setting time, difficult handling characteristics, and the potential to cause tooth discoloration. These are considered main drawbacks of MTA. (Macwan & Deshpande, 2014).

3.2.2. Biodentine

Biodentine is another calcium silicate–based bioceramic material that is widely used in vital pulp therapy. The main ingredients of Biodentine are tricalcium silicate, calcium carbonate, and zirconium oxide.

This material provides clinical advantages due to its short setting time, favorable mechanical properties, and high biocompatibility. Biodentine also promotes mineralization in the pulp tissue and contributes to the formation of a thick and homogeneous dentin bridge. (Nowicka et al., 2013).

Recent developments in bioceramic technology have led to the changings of materials designed to overcome some of the limitations associated with mineral trioxide aggregate (MTA) which are prolonged setting time and potential tooth discoloration. Among these materials, Biodentine has gained considerable attention due to its favorable physicochemical and biological properties. Biodentine shows a significantly shorter setting time (approximately 12 minutes), improved handling characteristics, and high compressive strength, which make it more convenient for clinical applications. Additionally, its bioactive nature promotes biomineralization and supports the formation of a thick and homogeneous dentin bridge. Researches have reported that Biodentine demonstrates superior clinical outcomes than MTA in certain vital pulp therapy procedures. These advantages have contributed to the increasing preference for Biodentine as an alternative to MTA in contemporary endodontic practice and also in recent years it has increasingly been preferred for pulp capping and pulpotomy procedures (Aksoy & Kocak, 2025).

3.3. Resin-modified calcium silicate-based materials (RM-CSMs)

Among the materials used in vital pulp therapy, resin-modified calcium silicate–based materials (RM-CSMs), including TheraCal LC and TheraCal PT, have gained increasing attention. Recent evidence suggests that resin-modified calcium silicate-based materials may demonstrate clinical success rates comparable to conventional calcium silicate materials during short-term follow-up. However, long-term outcomes appear to favor conventional bioceramic

materials such as MTA and Biodentine, particularly regarding dentin bridge formation and reparative dentinogenesis.

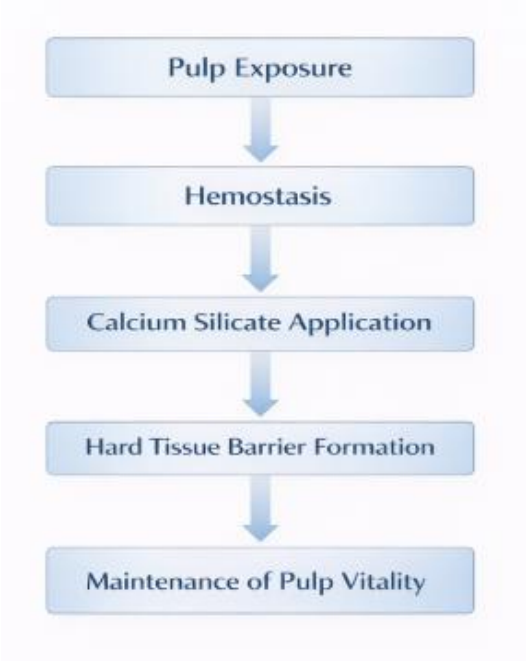
The reduced biological performance of some resin-modified calcium silicate materials has been attributed to the release of unpolymerized resin monomers, which may induce oxidative stress, compromise mitochondrial function, and negatively affect pulp cell viability (Cabrera-Fernández et al., 2026).

4. Calcium Silicate Applications in Vital Pulp Therapy

In recent years, significant advances have been made in the materials used for vital pulp therapy, and calcium silicate–based bioceramic materials have gained widespread use in clinical practice. The development of calcium silicate–based materials such as mineral trioxide aggregate (MTA) and Biodentine has increased the success rates of vital pulp therapies and enabled a more effective utilization of the biological healing capacity of the pulp tissue. (Camilleri, 2022; Parirokh et al., 2018).

Calcium silicate–based materials have high biocompatibility, ability to induce minimal inflammatory response in the pulp tissue and capacity to promote biomineralization. Because of these characteristics they are preferred in vital pulp therapy. During their setting reaction, they release calcium ions which support the formation of hydroxyapatite and contribute to the development of a protective mineralized tissue barrier over the pulp. (Camilleri, 2022)

Figure 1. Calcium silicate use in vital pulp therapy



Calcium silicate materials can also exhibit antibacterial effects due to their high pH values and help control bacterial contamination. Because of these reasons, they are frequently used today in direct pulp capping and pulpotomy procedures. (by: et al., 2019).

4.1. Resin-Modified Calcium Silicate Materials in Vital Pulp Therapy

Resin-modified calcium silicate–based materials (RM-CSMs) have been introduced in vital pulp therapy to combine the biological advantages of conventional calcium silicate cements with improved handling properties. These materials incorporate a resin component into the calcium silicate matrix, allowing light-curing capability, enhanced manipulation, and shorter setting times compared with traditional bioceramic materials.

TheraCal LC and **TheraCal PT** are widely used resin-modified calcium silicate materials in vital pulp therapy. They have been proposed as alternative materials for procedures such as indirect pulp capping, direct pulp capping, and pulpotomy. These materials provides immediate setting time because of their light-curing nature. Thus clinicians can complete restorative procedures more efficiently. In addition, their improved consistency and handling characteristics may facilitate easier placement during clinical procedures (Baranwal et al., 2024).

Despite these advantages, concerns have been raised regarding the biological performance of resin-modified calcium silicate materials. Researches show that the presence of resin components may effect their bioactivity and pulpal response. Releasing of unpolymerized resin monomers has been associated with increased cytotoxicity and reduced pulp cell viability when compared with conventional calcium silicate-based materials (Cabrera-Fernández et al., 2026).

Although short-term clinical outcomes of RM-CSMs appear to be comparable to mineral trioxide aggregate (MTA) and Biodentine, some studies have reported differences in long-term biological outcomes. In particular, the formation of a complete and homogeneous dentin bridge, which is considered a key indicator of pulpal healing, may occur less frequently with certain resin-modified materials (Mahapatra, Nikhade, Patel, Mankar, & Taori, 2024).

For these reasons, while resin-modified calcium silicate materials offer practical clinical advantages, conventional calcium silicate-based bioceramics remain the preferred option in situations where optimal bioactivity and predictable dentin bridge formation are essential. Continued research and long-term clinical trials are required to better clarify the biological performance and clinical indications of RM-CSMs in vital pulp therapy.

4.2. Direct Pulp Capping with Calcium Silicate

Direct pulp capping is a vital pulp therapy procedure aimed at preserving pulp vitality when the pulp tissue becomes exposed due to mechanical, traumatic, or caries-related causes. During direct pulp capping with calcium silicate, a biocompatible material is placed over the exposed pulp to promote pulp healing and stimulate the formation of a dentin bridge.

In the direct pulp capping procedure, bleeding at the site of pulp exposure should first be controlled. After hemostasis is achieved, a calcium silicate–based material is placed directly over the exposed pulp, and adequate coronal sealing is provided with an appropriate restorative material.

The literature has reported that MTA and Biodentine demonstrate high success rates in direct pulp capping procedures. (Nowicka et al., 2013).

4.3. Pulpotomy with Calcium Silicate

Pulpotomy is a vital pulp therapy procedure based on the partial or complete removal of the coronal pulp tissue while preserving the vitality of the radicular pulp. During pulpotomy with calcium silicate, a biocompatible material is applied

over the remaining pulp tissue to promote pulp healing and stimulate the formation of a mineralized tissue barrier.

Calcium silicate–based materials support the healing process by reducing inflammation in the pulp tissue. (Taha & Khazali, 2017).

Currently, pulpotomy procedures performed with calcium silicate–based materials have been reported to yield successful outcomes not only in primary teeth but also in permanent teeth. Further, some studies have shown that pulpotomy may be successful even in certain cases presenting with symptomatic pulpitis. (Bjørndal et al., 2019).

These developments have increased the importance of vital pulp therapies within modern endodontic treatment approaches and have contributed to the wider adoption of biologically based treatments aimed at preserving pulp vitality.

Table 1. Calcium Silicate Applications in Vital Pulp Therapy

Procedure	Clinical Indication	Clinical Steps	Expected Outcome
Direct Pulp Capping	Small mechanical or carious pulp exposure with controlled bleeding	Hemostasis → Placement of calcium silicate material (MTA/Biodentine) → Coronal restoration	Formation of a dentin bridge and maintenance of pulp vitality
Partial Pulpotomy	Traumatic pulp exposure or inflamed superficial pulp tissue	Removal of 1–2 mm superficial pulp → Hemostasis → Placement of calcium silicate material	Healing of remaining pulp tissue and continued root development
Full Pulpotomy	Extensive coronal pulp inflammation	Removal of coronal pulp → Hemostasis → Placement of calcium	Preservation of radicular pulp vitality

Procedure	Clinical Indication	Clinical Steps	Expected Outcome
	with vital radicular pulp	silicate material over radicular pulp	and mineralized barrier formation

Conclusion

Vital pulp therapies are conservative treatment approaches that aim to utilize the biological healing capacity of the pulp tissue. Today, the growing body of knowledge regarding pulp biology and healing mechanisms has significantly increased the importance of vital pulp therapies among endodontic treatment options. With appropriate case selection, correct clinical procedures and using of biocompatible materials, these treatments can achieve high success rates in preserving pulp vitality.

Procedures such as indirect pulp capping, direct pulp capping, and pulpotomy may apply in cases of deep carious lesions, mechanical or traumatic pulp exposures, and reversible pulpitis. They represent important treatment options which aim to preserve the pulp tissue.

Calcium silicate–based bioceramic materials developed in recent years have played a significant role in the success of vital pulp therapies. Materials such as mineral trioxide aggregate (MTA) and Biodentine have high biocompatibility, antibacterial properties, and ability to promote biomineralization, enable the formation of a more organized and stable dentin bridge within the pulp tissue. These advancements have contributed to more favorable clinical outcomes compared with the traditionally used calcium hydroxide materials.

The adoption of minimally invasive treatment approaches in modern endodontics has increased the importance of strategies aimed at preserving pulp vitality. When appropriate clinical conditions are provided, vital pulp therapies can achieve successful outcomes not only in young permanent teeth but also in permanent teeth with completed root development.

In conclusion, vital pulp therapies provide a biological approach aimed at preserving pulp tissue and occupy an important place in modern endodontic treatment concepts. Future developments in bioceramic materials and biologically based treatment methods focused on pulp regeneration are expected to further improve the clinical success rates of vital pulp therapies and expand their range of clinical applications.

REFERENCES

Aguilar, Panuroot, & Linsuwanont, Pairoj. (2011). Vital pulp therapy in vital permanent teeth with cariously exposed pulp: a systematic review. *Journal of endodontics, 37*(5), 581-587.

Aksoy, Duygu, & Kocak, Sibel. (2025). Management Strategies for Teeth with Open Apex: From Apexification to Regenerative Endodontics. *Cumhuriyet Dental Journal, 28*(3), 462-468.

Baranwal, Harakh Chand, Mittal, Neelam, Samad, Silviya, Ayubi, Aiyman, Aggarwal, Harshitaa, & Kharat, Shubham M. (2024). Comparative evaluation of dual-cure resin (TheraCal PT) and Biodentine in coronal pulpotomy of patients with symptoms indicative of irreversible pulpitis: A randomized clinical trial. *Journal of Conservative Dentistry and Endodontics, 27*(8), 822-827.

Barrett, Brenda, & O'Sullivan, Michael. (2021). Management of the deep carious lesion: a literature review. *Journal of the Irish Dental Association, 67*(1, February-March).

Berman, Louis H, & Hargreaves, Kenneth M. (2020). *Cohen's Pathways of the Pulp-E-Book: Cohen's Pathways of the Pulp-E-Book*: Elsevier Health Sciences.

Bjørndal, Lars, Simon, Stephane, Tomson, PL, & Duncan, HF. (2019). Management of deep caries and the exposed pulp. *International Endodontic Journal, 52*(7), 949-973.

by:, European Society of Endodontology developed, Duncan, HF, Galler, KM, Tomson, PL, Simon, S, El-Karim, I, . . . Fransson, H. (2019). European Society of Endodontology position statement: Management of deep caries and the exposed pulp. *International Endodontic Journal, 52*(7), 923-934.

Cabrera-Fernández, Alberto, Dominguez-Dominguez, Laura, Pérez-Pérez, Antonio, Santos, João Miguel Marques, Díaz-Cuenca, Aránzazu, Torres-Lagares, Daniel, . . . Martín-González, Jenifer. (2026). Clinical and Radiographic Outcomes of Vital Pulp Therapy Using Resin-Modified Versus Conventional Calcium Silicate-Based Materials: A Systematic Review and Meta-Analysis. *Journal of Functional Biomaterials, 17*(1), 32.

Camilleri, Josette. (2015). Mineral trioxide aggregate: present and future developments. *Endodontic Topics, 32*(1), 31-46.

Camilleri, Josette. (2022). Hydraulic calcium silicate-based endodontic cements. *Endodontic Advances and Evidence-Based Clinical Guidelines*, 311-346.

Cervino, Gabriele, Laino, Luigi, D'Amico, Cesare, Russo, Diana, Nucci, Ludovica, Amoroso, Giulia, . . . Gambino, Dario. (2020). Mineral trioxide aggregate

applications in endodontics: A review. *European journal of dentistry, 14*(04), 683-691.

Donnelly, Aisling, Foschi, Federico, McCabe, Paul, & Duncan, Henry F. (2022). Pulpotomy for treatment of complicated crown fractures in permanent teeth: A systematic review. *International Endodontic Journal, 55*(4), 290-311.

Duncan, Henry F. (2022). Present status and future directions—Vital pulp treatment and pulp preservation strategies. *International Endodontic Journal, 55*, 497-511.

Duncan, Henry F, Tomson, Philip L, Simon, Stephane, & Bjørndal, Lars. (2021). Endodontic position statements in deep caries management highlight need for clarification and consensus for patient benefit. *International Endodontic Journal, 54*(11), 2145-2149.

Emara, Ramy, Krois, Joachim, & Schwendicke, Falk. (2020). Maintaining pulpal vitality: cost-effectiveness analysis on carious tissue removal and direct pulp capping. *Journal of Dentistry, 96*, 103330.

Gomez-Sosa, Jose Francisco, Granone-Ricella, Mario, Rosciano-Alvarez, Marina, Barrios-Rodriguez, Victor D, Goncalves-Pereira, Juan, & Caviedes-Bucheli, Javier. (2024). Determining factors in the success of direct pulp capping: a systematic review. *The Journal of Contemporary Dental Practice, 25*(4), 392-401.

Kandemir Demirci, G, Kaval, ME, Güneri, P, & Çalışkan, MK. (2020). Treatment of immature teeth with nonvital pulps in adults: a prospective comparative clinical study comparing MTA with Ca (OH) 2. *International Endodontic Journal, 53*(1), 5-18.

Louzada, Lidiane M, Hildebrand, Hauke, Neuhaus, Klaus W, & Duncan, Henry F. (2025). The effectiveness of partial pulpotomy compared with full pulpotomy in managing deep caries in vital permanent teeth with a diagnosis of non-traumatic pulpitis. *International Endodontic Journal, 58*(1), 37-54.

Macwan, Chirag, & Deshpande, Anshula. (2014). Mineral trioxide aggregate (MTA) in dentistry: A review of literature. *Journal of Oral Research and Review, 6*(2), 71-74.

Mahapatra, Joyeeta, Nikhade, Pradnya P, Patel, Aditya, Mankar, Nikhil, & Taori, Prachi. (2024). Comparative evaluation of the efficacy of TheraCal LC, mineral trioxide aggregate, and biodentine as direct pulp capping materials in patients with pulpal exposure in posterior teeth: a triple-blinded randomized parallel group clinical trial. *Cureus, 16*(2).

Marques, Miguel Seruca, Wesselink, Paul R, & Shemesh, Hagay. (2015). Outcome of direct pulp capping with mineral trioxide aggregate: a prospective study. *Journal of endodontics, 41*(7), 1026-1031.

Mente, Johannes, Geletneky, Beate, Ohle, Marc, Koch, Martin Jean, Ding, Paul Georg Friedrich, Wolff, Diana, . . . Pfefferle, Thorsten. (2010). Mineral trioxide aggregate or calcium hydroxide direct pulp capping: an analysis of the clinical treatment outcome. *Journal of endodontics, 36*(5), 806-813.

Nowicka, Alicja, Lipski, Mariusz, Parafiniuk, Mirosław, Sporniak-Tutak, Katarzyna, Lichota, Damian, Kosierkiewicz, Anita, . . . Buczkowska-Radlińska, Jadwiga. (2013). Response of human dental pulp capped with biodentine and mineral trioxide aggregate. *Journal of endodontics, 39*(6), 743-747.

Parirokh, Masoud, Torabinejad, M, & Dummer, PMH. (2018). Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview–part I: vital pulp therapy. *International Endodontic Journal, 51*(2), 177-205.

Ramani, Ankita, Sangwan, Pankaj, Tewari, Sanjay, Duhan, Jigyasa, Mittal, Shweta, & Kumar, Vinay. (2022). Comparative evaluation of complete and partial pulpotomy in mature permanent teeth with symptomatic irreversible pulpitis: a randomized clinical trial. *International Endodontic Journal, 55*(5), 430-440.

Raoof, Maryam, Vazavandi, Elahe, Parizi, Molook Torabi, Hatami, Nima, Mohammadalizadeh, Sakineh, Amanpour, Sara, & Haghani, Jahangir. (2022). Clinical, radiological, and histological correlation in diagnosis of pulpitis. *Dental Research Journal, 19*(1), 25.

Sachdeva, Akshat, Kumar, Vishal, Chawla, Amrita, Priya, Harsh, Kumar, Vijay, Sharma, Sidhartha, & Logani, Ajay. (2025). Quality assessment of clinical practice guidelines and position statements on vital pulp therapy: a systematic review. *Evidence-Based Dentistry, 26*(2), 115-116.

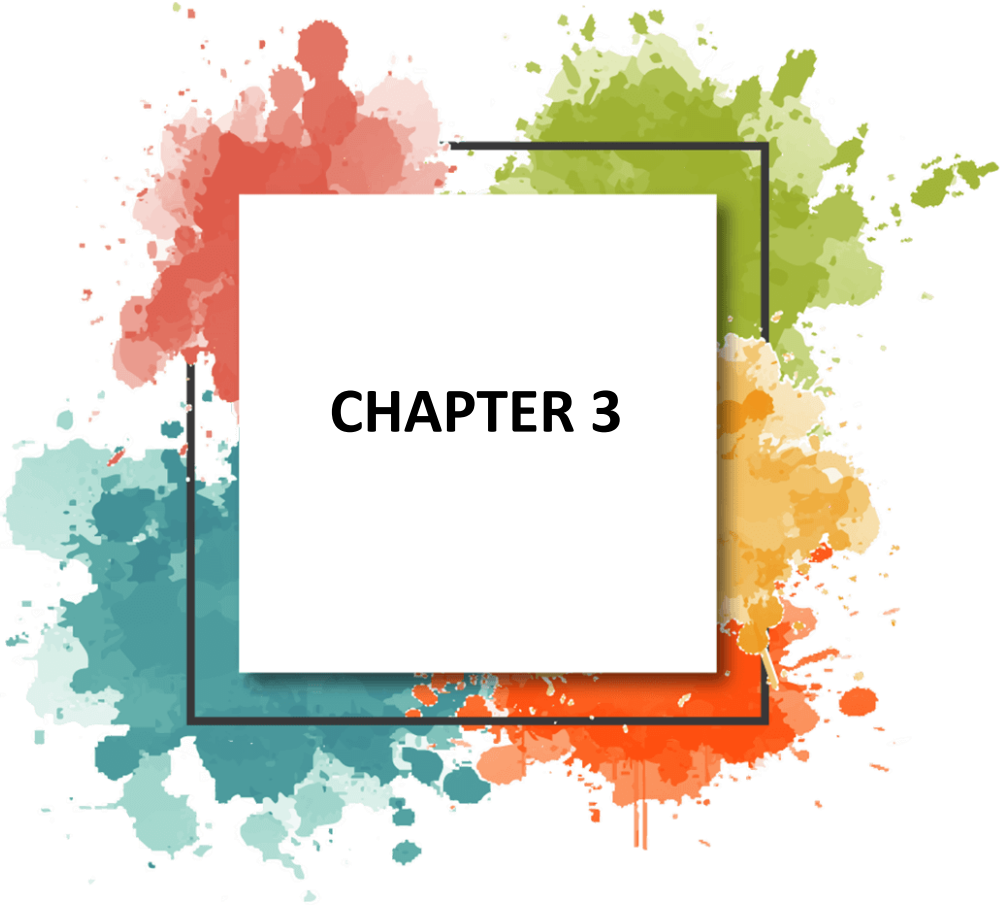
Schwendicke, Falk, & Göstemeyer, Gerd. (2016). Understanding dentists' management of deep carious lesions in permanent teeth: a systematic review and meta-analysis. *Implementation Science, 11*(1), 142.

Taha, Nessrin A, & Albakri, Shurouq W. (2024). Outcome and prognostic factors for partial and full pulpotomy in the management of spontaneous symptomatic pulpitis in carious mature permanent teeth: a randomized clinical trial. *Journal of endodontics, 50*(7), 889-898.

Taha, Nessrin A, & Khazali, Mohammad A. (2017). Partial pulpotomy in mature permanent teeth with clinical signs indicative of irreversible pulpitis: a randomized clinical trial. *Journal of endodontics, 43*(9), 1417-1421.

Warreth, Abdulhadi. (2023). Dental caries and its management. *International Journal of Dentistry, 2023*(1), 9365845.

Witherspoon, David E. (2008). Vital pulp therapy with new materials: new directions and treatment perspectives—permanent teeth. *Pediatric dentistry, 30*(3), 220-224.


CHAPTER 3

PRINCIPLES OF VITAL PULP THERAPY

Gülçin Cagay Sevencan[1]

1. Principles of Vital Pulp Therapy

Vital pulp therapies are methods aimed at preserving function of the dental pulp and the vitality in cases where damage has occurred due to caries, trauma, or restorative procedures. Recent studies revealing the pulp's defense mechanisms and healing continuity are leading to a significant transformation in their treatment (Coll et al., 2024; El Karim et al., 2021). VPT procedures have traditionally been considered to include indirect pulp capping or direct pulp capping, as well as partial or complete pulpotomy (Endodontists, 2003). In immature permanent teeth, VPT allows root formation to continue by maintaining continuous vitality and is recommended for traumatic pulp exposures where inflammation is superficial, as observed in histological analysis (Kahler et al., 2023).

Mature teeth were previously considered irreversibly inflamed following carious pulp exposure, and RCT was recommended. This is attributed to a long-term study using calcium hydroxide, which reported negative outcomes in pulp capping treatment for most cases of carious pulp exposure (Barthel et al., 2000). This negative outcome likely resulted not from the procedure itself, but rather from suboptimal infection control protocols and compromised coronal seal integrity (Kahler et al., 2023).

Teeth with caries exposure and a diagnosis of irreversible pulpitis have reported similar outcomes in randomized controlled trials (Asgary et al., 2015; Asgary et al., 2022). However, there are studies reporting rapid pain relief following pulpotomy treatment, which is well-tolerated by patients (Galani et al., 2017). Therefore, treating the tooth with pulpotomy rather than the RCT approach offers an advantage for the patient. It has been reported that VPT is a simple and more cost-effective strategy compared to traditional mechanical approaches such as pulpectomy and root canal therapy (Schwendicke & Herbst, 2023). Potentially, the retreatment of a failed pulpotomy may be easier than the retreatment of a tooth with a root filling (Kahler et al., 2023). VPT is currently recognized as an accepted method for symptomatic carious teeth by the European Society of

[1] Assistant Prof. Dr. Department of Endodontics, Faculty of Dentistry, Tekirdag Namık Kemal University, Tekirdag, Turkey. ORCID No: 0000-0002-8486-4572

Endodontology (ESE) (by: et al., 2019) and the American Association of Endodontists (AAE) (Craig S. Hirschberg et al., 2021).

The ESE defines vital pulp therapy as strategies aimed at preserving the health of all or part of the pulp (by: et al., 2019). The American Association of Endodontists has described vital pulp therapy as methods aimed at preserving the vitality and function of the dental pulp following damage caused by trauma, caries, or restorative procedures (Craig S. Hirschberg et al., 2021).

1.1. Diagnosis

When it comes to vital pulp therapy, it is considered particularly important that the treatment be recommended and performed only after a definitive diagnosis has been established.

Traditionally, in endodontics, the diagnosis of pulp diseases depends on the clinician's assessment of the patient's pain history combined with the application of suitable clinical tests to evaluate the status of the pulp; such as cold stimulation and electrical pulp testing. Since tests that definitively determine pulp viability, such as pulp oxygen tension measurement are not presently accessible for clinical application (Chen & Abbott, 2009). An initial positive reaction to a pulp sensitivity test is indicative of a more advanced stage of pulp inflammation. This response is defined as a "prolonged" and intense reaction to a cold stimulus. Underlying this are pathophysiological mechanisms such as c-fiber sensitization and hypersensitivity caused by inflammation (Diogenes & Henry, 2012). In addition to pulp sensitivity tests, percussion tests can predict pulp status in cases of symptomatic apical periodontitis. The existence of percussion pain can indicates that the pulp is in a state of irreversible inflammation (Owatz et al., 2007).

To accurately assess the degree of root formation, other accompanying hard tissue changes, and periradicular or furcation changes, diagnostic-quality intraoral radiographs of suspect teeth are recommended (McDonald et al., 2010). The diagnostic terminology established by the AAE categorizes vital pulp into three distinct classifications: "normal," "reversible pulpitis," and "irreversible pulpitis," (which may be asymptomatic or symptomatic) (Levin et al., 2009).

The diagnosis of reversible versus irreversible pulpitis in immature teeth is often complicated by subjective symptoms and diagnostic test responses that represent the histopathological characteristics of pulp tissue (Souza et al., 2007). The treatment approach for these teeth should aim to preserve the tooth's vitality and facilitate the continuation of apogenesis in immature teeth (Bogen & Chandler, 2008).

Patients with teeth affected by deep carious lesions often exhibit sensitivity to thermal stimuli such as cold and hot, as well as to sweet, or acidic foods and may elicit a brief, persistent response lasting 1–2 seconds during a cold test (Berman & Hargreaves, 2020). Clinical studies indicate that the pulp sensitivity test using carbon dioxide ice in the cold test is a more reliable prognostic tool compared to electronic testing devices. However, teeth with a positive percussion test may be evaluated as having irreversible pulpitis or necrosis (Bogen & Chandler, 2010).

Accurate diagnosis of pulp disease remains a significant challenge. Nonetheless, the validity of these classifications has been challenged in histological investigations (Ricucci et al., 2014). These studies have revealed that a definitive differentiation between reversible and irreversible pulpitis cannot be established solely on the basis of patients' clinical symptoms. In their study, Ricucci et al. reported that 84% of teeth clinically diagnosed with irreversible pulpitis were consistent with irreversible pulpitis based on histological findings, while 16% exhibited mild inflammation or normal histology. This suggests that performing root canal treatment on some cases clinically diagnosed as irreversible pulpitis would constitute overtreatment (Ricucci et al., 2014). Additionally, in these teeth consistent with the clinical diagnosis, it is notable that, upon histological examination, the infection is confined to a region of variable dimensions beneath the exposed region. It is highly likely to find normal pulp tissue in part of the pulp chamber or within the root canal. Therefore, it has been demonstrated that such teeth can be effectively managed through either partial or complete pulpotomy. (Kahler et al., 2023; Ricucci et al., 2014).

Assessing the irreversibility of pulp disease presents a significant challenge when considering clinical, biological, and theoretical factors (Rechenberg & Zehnder, 2020). Histological evidence regarding the progression of pulpitis indicates that there is no distinct boundary that would render the pulp irreparable (Ricucci et al., 2019). Rather, pulpitis can be interpreted as a disease graded temporally and spatially, and some have proposed the following terms for grading: "initial," "mild," "moderate," and "severe pulpitis" (Rechenberg & Zehnder, 2020).

Current research efforts are focused on the role of inflammatory mediators in more accurately representing the status of the dental pulp (Zanini et al., 2017). For example, point-of-care diagnostic techniques using dentin fluid (Zehnder et al., 2011) (without pulp exposure) or pulp blood (Mente et al., 2016) (when pulp exposure is present) have been demonstrated to detect biomarkers indicative of tissue degradation, including matrix metalloproteinase-9. Although there are recommendations regarding the use of biomarkers in the diagnosis of pulp, established threshold values supporting routine use in clinical practice are not yet available (Duncan et al., 2023).

In the absence of routinely accessible molecular biological tests in clinics, direct observation of the pulp tissue, using a surgical microscope is is recommended as a valuable diagnostic approach. It can provide relevant information to determine the case's suitability for VPT. Firstly, it enables the correct diagnosis of necrotic pulp that may have been previously misdiagnosed. Secondly, observing the pulp tissue during and following hemostasis offers supplementary diagnostic insights into the pulp's condition. Using direct observation of the pulp, even symptomatic pulp appears to be a candidate for VPT (Craig S. Hirschberg et al., 2021; Lin et al., 2020).

1.2. Removal of Caries

In vital pulp therapies, it has traditionally been stated that complete removal of infected tissues and caries is necessary to allow visualization of the pulp status under magnification in cases of carious pulp exposure (Craig S. Hirschberg et al., 2021). Since residual caries, varying levels of pulp inflammation, and potential areas of necrosis may jeopardize adequate observation of the pulp, it has been suggested that vital pulp therapy may not be appropriate without complete removal of demineralized enamel and infected dentin. Dentin located beneath white enamel lesions or within hard dentin may be infected by bacteria in both active and quiescent lesions. Histological researchs have demonstrated the presence of chronic inflammatory cell infiltration and signs of subclinical pulpitis in the pulp tissue associated with carious lesions. This condition potentially jeopardize pulp vitality (Ricucci & Siqueira Jr, 2020; Ricucci et al., 2020).

Traditionally, caries removal is completed in a somewhat subjective manner using hand instruments and slow or high-speed drills. The procedure suggests distinguishing between infected and non-infected tooth structure using a probe and tactile sensitivity. A limitation of these methods is that they may leave caries behind, including at the enamel-dentin junction, or lead to the unnecessary removal of tissue that has the potential to remineralize (Berman & Hargreaves, 2020). Additionally, methods using caries-detecting dye and optical magnification have been developed to ensure the complete removal of caries and infected tissue while preserving healthy tooth structure; however, it has been determined that these methods may also lead to the unnecessary removal of healthy tooth tissue (Banerjee et al., 2000).

The use of laser fluorescence during caries removal has been described as a supportive tool that assists in removing infected tissues, particularly in areas near the pulp chamber (Hosoya et al., 2007). Therefore, instead of attempting to prevent pulp exposure to enhance the likelihood of successful pulp preservation, the clinician can focus on the thorough removal of infected and demineralized dentin (Langeland, 1981). Caries detection tools have the potentional to provide

a standartized and objective criterion for clinicians during removal of caries lesions, independent of subjective judgment.

Contemporary management strategies for pulp exposed to caries have led to the resurgence of VPT techniques, including both partial and full pulpotomy procedures (Simon et al., 2013). Given that maintaining pulp vitality and preventing apical periodontitis, are a fundamental principle of endodontics, these advancements form the foundation of the profession. Due to the destructive nature of traditional dental treatments, a minimally invasive approach is gaining prominence in dentistry. ESE discusses the treatment of extensive caries lesions, which are classified into two radiographic categories: deep caries and extremely deep carious (by: et al., 2019). Deep carious lesions reach the inner quarter of the dentin, however, a region of hard or solid dentin region detectable radiographically exists between the lesion and pulp. Extremely deep caries lesions, however, penetrate the full thickness of the dentin both clinically and radiographically (Bjørndal et al., 2019). It has been noted that the treatment of deep caries has shifted from non-selective (complete) caries removal to a selective approach, thereby minimizing the risk of pulp exposure. (by: et al., 2019; Innes et al., 2016)

Uncertainty persists regarding the optimal endpoint of caries removal in deep lesions (Dhar et al., 2026). In particular, there is a need to identify reliable biomarkers capable of predicting the success of conservative treatment. Furthermore, prospective studies comparing the long-term clinical outcomes of selective and complete caries removal are of great importance, given the ongoing paradigm shift toward more conservative treatment strategies (Duncan et al., 2023; Maltz et al., 2012)

Following confirmation of pulp vitality, evaluation of the stage of root development, and consideration of the feasibility of placing a well-sealed restoration, clinicians are encouraged to adopt a conservative approach in the management of deep carious lesions in permanent teeth (Dhar et al., 2026). Except for extremely deep lesions, selective caries removal or stepwise excavation is recommended over non-selective (complete) caries removal. In addition, selective caries removal offers the practical advantage of being completed in a single visit. These recommendations are also emphasized in the Consensus-Based Recommendations on Pulp Therapy for Primary and Permanent Teeth: IAPD Porto Forum, published by the International Association of Paediatric Dentistry (Dhar et al., 2026). However, clinical decision-making should be individualized, taking into account factors such as lesion depth, clinical and radiographic assessment of pulpal status, and restorative considerations.

1.3. Hemostatic Agents

A wide variety of agents have been recommended to control bleeding in cases of bleeding pulp. These include various concentrations of NaOCl, MTAD (Dentsply, Tulsa, OK), 2% CHX, ferric sulfate, 30% hydrogen peroxide, and disinfectants such as Tubulicid (Global Dental Products, North Belmore, NY), epinephrine, sterile water, the application of direct pressure using cotton pellets saturated with saline, and the utilization of laser technology (Berman, 2020). NaOCl at concentrations ranging from 1.5% to 5.25% currently stands out as the most reliable, cost-effective, and efficient method (Berman & Hargreaves, 2020). The antimicrobial solution facilitates hemostasis and disinfection of the dentin-pulp interface, chemical lysis of blood clots and fibrin, aids in biofilm removal, cleanses dentin debris, and eliminates damaged cells in the pulp exposure area. NaOCl concentrations between 1.5% and 5.25% do not appear to adversely affect cell differentiation or hard tissue formation. Washing the pulp with 5 mL of NaOCl for 15 minutes leads to dissolution effects. This dissolution is limited to the 3–5-layer upper cell layer rather than deep pulp tissue (Berman & Hargreaves, 2020).

Pulpal hemostasis generally achieved by applying sodium hypochlorite to the amputated pulp tissue for a duration of 5 to 10 minutes. This clinical step can be executed by using sodium hypochlorite-soaked cotton pellets or by employing passive irrigation techniques (Craig S. Hirschberg et al., 2021).

The ability to achieve hemostasis upon pulp exposure is one of the most important factors influencing the success of vital pulp therapy. A 2-year clinical study supported the use of a caries detector dye containing 10% NaOCl (Matsuo et al., 1996). The success rate was found to be 81.8% at the 2-year follow-up. Analysis of factors influencing success revealed that preoperative pain, percussion sensitivity, thermal response, opening diameter, patient age, tooth location and type, had no effect on the treatment outcome.

1.4. Points to Consider in Vital Pulp Treatments

Even after the decay has been removed from a decayed area, bacteria may persist in the tubules near the perforation site. These microorganisms can compromise the treatment even with meticulous work and thorough caries removal. Therefore, the clinician should work under rubber dam isolation during vital pulp therapy and seal not only the perforation site but also the surrounding dentin with calcium silicate-based cement (CSC) to address potential residual bacteria (Yoo et al., 2016).

In VPTs, a sufficient CSC material must be placed onto the pulp to create a leak-proof barrier. Application of these materials in sufficient thickness over the pulp is essential to ensure physical durability and long-term hermetic sealing

(Haapasalo et al., 2015). The strategic placement of hydraulic CSCs is vital to provide an effective barrier against bacterial microleakage, thereby facilitating pulpal repair (Duncan et al., 2023).

Both Biodentin and MTA exhibit similar clinical and radiographic efficacy as pulpotomy agents in mature permanent teeth with exposed decayed pulp. Considering its favorable ease of application and reduced risk of discoloration, Biodentin may serve as a viable alternative to MTA. (Soma et al., 2025). Higher-quality studies are needed to strengthen the current evidence base.

A meta-analysis study showed that the use of ProRoot MTA resulted in a significant increase in the frequency of complete hard tissue bridge formation, hard tissue thickness, and morphology when compared to various other CSCs and calcium hydroxide (Silva et al., 2025). It was noted that this scenario is not clinically representative and therefore the results should be interpreted with caution (Silva et al., 2025).

A meta-analysis and systematic review of vital pulp treatment options in permanent teeth revealed the following results: Selective caries removal minimized pulp exposuring in deep caries diagnosed with normal pulp and reversible pulpitis (Coll et al., 2025). For teeth diagnosed with symptomatic irreversible pulpitis or excessively deep caries, complete pulpotomy is recommended after complete caries removal to remove the pulp, provided a pulp bleeding control panel is obtained. However, maintaining hemostasis within six minutes during this time increases the likelihood of pulpotomy (Coll et al., 2025). Mineral trioxide aggregates, bismuth oxides, and Biodentine (zero percent) show significantly more discoloration (83%). Partial pulpotomy or complete pulpotomy has been shown to be significantly more successful than direct pulp capping in traumatic pulp exposures (Coll et al., 2025). Root maturity has been suggested to be unaffected by partial or complete pulpotomy in teeth with normal pulp or reversible pulpitis. Consequently, this meta-analysis revealed that all vital pulp treatment methods in permanent teeth are successful for teeth diagnosed with normal pul por reversible pulpitis, but symptomatic irreversible pulpitis can only be successfully treated with complete pulpotomy (Coll et al., 2025).

In vital pulp therapy, it is essential that the materials employed exhibit high sealing ability and establish a strong bond with the composite in order to maintain the viability of the pulp tissue. TheraCal LC material, a resin-based CSC, has shown bond strength similar to that of Biodentine. However, TheraCal PT, a pulpotomy treatment material, is promising due to its good sealing properties and good bonding to bulk-fill composites. (Falakaloğlu et al., 2023).

Consensus-based recommendations indicate that vital pulp treatment (VPT) in permanent teeth with deep caries should primarily involve the use of CSCs

(Cooper et al., 2014). This is because these biomaterials promote pulp healing and support reparative dentin formation, improving long-term treatment outcomes (Dhar et al., 2026).

In cases where pulp is not exposed, glass ionomer cement may be considered, and placement of a well-sealed coronal restoration is essential for treatment success. In healthy teeth or teeth diagnosed with reversible pulpitis, selective caries removal (IPT) is recommended for deep, but not excessively deep, caries lesions (Dhar et al., 2026; Zanini et al., 2017).

In cases of pulp exposure, particularly when using CSCs, direct pulp capping (DPC) can be performed, but its long-term success is lower than pulpotomy (Dhar et al., 2026). In extremely deep caries with exposed pulp, partial or complete pulpotomy using CSCs shows high success rates and, if hemostasis is achieved, can be considered even in cases of irreversible pulpitis without signs of necrosis (Dhar et al., 2026). Complete pulpotomy can be used as a minimally invasive alternative to root canal treatment in mature permanent teeth with comparable success rates in selected cases (Asgary et al., 2015). In immature permanent teeth, complete pulpotomy is recommended to preserve pulp viability and support root development (Dhar et al., 2026). For immature and mature permanent teeth with non-traumatic pulpitis presenting with no or non-spontaneous pain, selective or stepwise caries removal without pulp exposure can be considered. If pulp exposure occurs, treatment options may include direct pulp capping or partial/full pulpotomy (Duncan et al., 2023).

For immature necrotic teeth, both apexification and regenerative endodontic treatments (RET) are viable options, and CSCs are preferred over calcium hydroxide-based approaches (Dhar et al., 2026).

2. Treatment Recommendations

Pulp capping and pulpotomy

Deep local anesthesia must be administered. The clinical crown of the tooth is disinfected with NaOCl or CHX after rubber dam isolation. Optical magnification and illumination (ideally using a dental operating microscope) are strongly recommended. The cavity is prepared using high-speed handpieces with continuous water cooling (Bogen & Chandler, 2008).

For caries removal, a micromotor with long-shank round burs (sizes 2–6) should be used. If a dental operating microscope is used, a caries detection dye may be applied prior to caries removal (Berman, 2020).

Rinsing the cavity and perforation sites with 1.5% to 5.25% NaOCl is recommended. If there is severe bleeding from the perforation site, a cotton pellet soaked in NaOCl is left in place for 5 minutes under moderate pressure (Berman

& Hargreaves, 2020). If there is no bleeding after the pulp is exposed, the pulp must be examined for necrotic tissue. This tissue is removed using a high-speed round bur under water cooling until bleeding occurs. During the procedure, following debridement, it is advisable to directly visualize the exposed pulp under magnification. The optimal characteristics of a healthy pulp wound include continuous tissue with adequate blood supply, encircled by clean and intact dentin. (Kahler et al., 2023).

If necrotic tissue, dentin remnants, or infected tissue that appears yellowish is present within the pulp, a partial pulpotomy should be conducted to excise the compromised tissue. Subsequently, the pulp wound should be reevaluated to determine whether the need for additional tissue removal is necessary and whether a transition from partial to complete pulpotomy is required (Kahler et al., 2023).

There are no contraindications based on the extent of pulp exposure for partial or complete pulpotomy. The distinction pertains to the extent or orientation of pulp tissue excision. In the instance of a partial pulpotomy involving a single exposure, tissue may be excised to a depth of 2 mm extending toward the base of the exposed region. Conversely, when two exposures are present, a horizontal partial pulpotomy may be conducted to link the two exposure sites and remove the underlying 2 mm of pulp tissue (Kahler et al., 2023).

Following a partial or complete pulpotomy, the pulp tissue structure should appear healthy, with no residual infected or necrotic tissue or dentin. This should be examined and confirmed using magnification thereafter hemostasis has been achieved. If hemostasis cannot be achieved, a pulpectomy should be performed (Kahler et al., 2023). The key consideration in deciding on VPT is that the amount of bleeding resulting from pulp exposure must be controlled to allow for the placement of hydraulic CSCs in the exposed area (Kahler et al., 2023).

Complete removal of all necrotic tissue is of critical importance. If bleeding continues uncontrollably 10 minutes after tissue removal, a decision to perform a complete pulpotomy or pulpectomy may be made based on the condition of the periapical region (Berman & Hargreaves, 2020).

After CSC (CSC) or MTA is prepared according to the manufacturer's instructions, it should be placed using an appropriate instrument (MTA applicator gun). Including the dentin surrounding the perforation, a sufficient amount of CSC should be placed in the exposed area to a thickness of 1.5–3 mm (Berman & Hargreaves, 2020). Subsequently, moisture in the area should be removed with a dry cotton pellet to prepare for the adhesive bonding. The use of phosphoric acid gel—one of the adhesive steps—is not recommended at this stage, as it would cause the MTA or CSC to wash away before setting (Bogen & Chandler,

2008). Instead, a fast-setting CSC (Biodentin) or a flowable composite or resin-modified glass ionomer cement material should be properly placed to completely cover the pulp capping material. A small amount of light-curing flowable compomer, resin-modified glass ionomer cement, self-etch, self-bonding flowable composite resin, or a flowable composite used in combination with self-etch should be applied to cover the DCA and light-cured for the recommended duration (Berman & Hargreaves, 2020).

The remaining cavity walls are etched for 60 seconds with 34% or 37% phosphoric acid gel, thoroughly rinsed, and then a dentin adhesive can be applied. Fourth-generation two-bottle systems are strongly recommended over single-bottle self-etch systems (Bogen & Chandler, 2008, 2010). They should be light-cured according to the manufacturer's instructions. A permanent restorative material is placed in stages and light-cured according to the manufacturer's instructions.

ESE has established two classes for direct pulp capping: Class I: Cases where no deep carious lesion is present preoperatively. Class II: Cases where a deep or extremely deep carious lesion is present preoperatively. Cases where pulp exposure occurs clinically over a region of bacterial contamination and inflammation of the underlying pulp tissue is expected (by: et al., 2019).

Pulp vitality should be assessed within 7 to 10 days, preferably using a cold test. In cases of a negative sensitivity test, radiographic follow-up should be performed annually. Evaluations should be conducted annually, or twice a year if necessary (Bogen & Chandler, 2008, 2010).

3. Permanent restorations

The success rate is high for teeth treated with VPT that are restored immediately with a long-term restoration using CSCs as the primary sealing material (Asgary et al., 2018; Brizuela et al., 2017; Taha & Abdulkhader, 2018). Although studies have shown that delayed final restoration yields some success in the short and medium term (Linsuwanont et al., 2017; Marques et al., 2015) long-term evaluations have shown that the duration between pulp therapy and the placement of the primary restoration (Tan et al., 2020) is a strong predictor of successful outcomes (Çalışkan & Güneri, 2017; Parirokh et al., 2018; Taha & Khazali, 2017).

There are several advantages to performing the permanent restoration immediately. These include preventing microleakage, preserving the biomaterial layer, reducing postoperative sensitivity and thermal conductivity, and providing a foundation for a cusp-covering restoration if necessary. No adverse effects of immediate tooth restoration have been reported. It is advisable to observe a suitable waiting period before proceeding with further tooth preparation for cusp-

covering restorations. The dentist should evaluate the tooth's readiness for definitive restoration following the completion of vital pulp therapy (VPT) by confirming the absence of clinical signs and symptoms, as well as assessing the tooth's tendency to fracture (Craig S. Hirschberg et al., 2021).

4. Postoperative Follow-Up

It is recommended that patients undergo evaluation at 6 and 12 months post-operative for ESE VPT procedures, followed by annual evaluations for 4 years (if necessary) (by: et al., 2019). The tooth is expected to exhibit a normal positive response to a pulp sensitivity test. However, it is recognized that certain teeth may not respond, such as those in elderly patients, teeth with multi-surface resin-based composite or ceramic restorations, and teeth that have undergone complete pulpotomy, which are not anticipated to respond to the test. (by: et al., 2019).

After vital pulp therapy for pulpitis and nonsurgical or surgical treatment of apical periodontitis, cases should be monitored over an extended period, with follow-up intervals prolonged when the healing outcome is uncertain (Duncan, at all. 2023).

Conclusion

Success in vital pulp treatments can be directly achieved through accurate diagnosis, appropriate caries removal strategy, effective hemostasis, non-releasing restoration with biocompatible materials, and regular clinical/radiographic follow-up. According to current data, selective caries removal in deep caries reduces pulp exposure, while controlled exposure of the required amount results in highly successful vital pulp treatments with reproducible results. Hemostasis is reported to be a particularly critical prognostic factor, and the success of pulpotomy with intermittent bleeding control is enhanced. Furthermore, the use of irrigation agents such as sodium hypochlorite for hemostasis and disinfection is also important.

Treatments with calcium silicate-based bioceramic materials (e.g., MTA, Biodentine) have been reported to show more predictable healing and higher success rates. In the restorative phase, maintaining a non-releasing coronal covering is essential for long-term success. Indirect pulp treatment, direct pulp placement, and pulpotomy, when applied in appropriate indications, are seen to have high success rates. However, it should be noted that in chronic, irreversible pulpitis, the success rate of the system is lower, and case selection is critically important. Consequently, success in vital pulp treatments depends not only on the material used but also on a holistic clinical approach that includes accurate diagnosis and caries removal, effective hemostasis, appropriate restoration, and regular follow-up. In principle, vital pulp treatments, which are suitable for these

diseases, stand out as a highly successful, reliable, and biological treatment option in modern endodontics.

ABBREVIATIONS

AAE: American Association of Endodontists

CHX: Chlorhexidine

CSC: Calcium silicate-based cement

DCA: Dichloroacetic acid

ESE: European Society of Endodontology

IAPD: International Association of Paediatric Dentistry

MTA: Mineral Trioxide Aggregate

MTAD: Mixture of Tetracycline isomer, Acid, and Detergent

NaOCl: Sodium hypochlorite

VPT: Vital pulp therapy(ies)

RET: Regenerative endodontic treatments

RCT: Root canal therapy

REFERENCES

Asgary, S., Eghbal, M. J., Fazlyab, M., Baghban, A. A., & Ghoddusi, J. (2015). Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial. *Clinical oral investigations*, *19*(2), 335-341.

Asgary, S., Eghbal, M. J., Shahravan, A., Saberi, E., Baghban, A. A., & Parhizkar, A. (2022). Outcomes of root canal therapy or full pulpotomy using two endodontic biomaterials in mature permanent teeth: a randomized controlled trial. *Clinical oral investigations*, *26*(3), 3287-3297.

Asgary, S., Hassanizadeh, R., Torabzadeh, H., & Eghbal, M. J. (2018). Treatment outcomes of 4 vital pulp therapies in mature molars. *Journal of endodontics*, *44*(4), 529-535.

Banerjee, A., Kidd, E., & Watson, T. (2000). In vitro evaluation of five alternative methods of carious dentine excavation. *Caries research*, *34*(2), 144-150.

Barthel, C. R., Rosenkranz, B., Leuenberg, A., & Roulet, J.-F. (2000). Pulp capping of carious exposures: treatment outcome after 5 and 10 years: a retrospective study. *Journal of endodontics*, *26*(9), 525-528.

Berman, L. H., & Hargreaves, K. M. (2020). *Cohen's Pathways of the Pulp-E-Book: Cohen's Pathways of the Pulp-E-Book*. Elsevier Health Sciences.

Bjørndal, L., Simon, S., Tomson, P., & Duncan, H. (2019). Management of deep caries and the exposed pulp. *International endodontic journal*, *52*(7), 949-973.

Bogen, G., & Chandler, N. P. (2008). Vital pulp therapy. *Ingle's endodontics*, *6*, 1310-1329.

Bogen, G., & Chandler, N. P. (2010). Pulp preservation in immature permanent teeth. *Endodontic topics*, *23*(1), 131-152.

Brizuela, C., Ormeño, A., Cabrera, C., Cabezas, R., Silva, C. I., Ramírez, V., & Mercade, M. (2017). Direct pulp capping with calcium hydroxide, mineral trioxide aggregate, and biodentine in permanent young teeth with caries: a randomized clinical trial. *Journal of endodontics*, *43*(11), 1776-1780.

by:, E. S. o. E. d., Duncan, H., Galler, K., Tomson, P., Simon, S., El-Karim, I., Kundzina, R., Krastl, G., Dammaschke, T., & Fransson, H. (2019). European Society of Endodontology position statement: Management of deep caries and the exposed pulp. *International endodontic journal*, *52*(7), 923-934.

Chen, E., & Abbott, P. V. (2009). Dental pulp testing: a review. *International Journal of Dentistry*, *2009*(1), 365785.

Coll, J. A., Dhar, V., Chen, C.-Y., Crystal, Y. O., Guelmann, M., Marghalani, A. A., AlShamali, S., Xu, Z., Glickman, G. N., & Wedeward, R. (2024). Use of vital pulp therapies in primary teeth 2024. *Pediatric Dentistry*, *46*(1), 13-26.

Coll, J. A., Dhar, V., Guelmann, M., Crystal, Y. O., Chen, C.-Y., Marghalani, A. A., AlShamali, S., Xu, Z., Glickman, G., & Ather, A. (2025). Vital pulp therapy in permanent teeth: a systematic review and meta-analyses. *Pediatric Dentistry*, *47*(3), 137-150.

Cooper, P. R., Holder, M. J., & Smith, A. J. (2014). Inflammation and regeneration in the dentin-pulp complex: a double-edged sword. *Journal of endodontics*, *40*(4), S46-S51.

Craig S. Hirschberg, D., Chair; George, Bogen, D. J. C. G., DMD, MS,, PhD; Ronald R. Lemon, D. O. A. P., DMD, M., PhD; Nikita B. Ruparel, DMD, MS,, PhD; Franklin R. Tay, B., PhD; and David E., & Witherspoon, B., MS. (2021). AAE Position Statement on Vital Pulp Therapy. *Journal of endodontics*, *47*(9), 1340-1344. https://doi.org/doi:10.1016/j.joen.2021.07.015

Çalışkan, M. K., & Güneri, P. (2017). Prognostic factors in direct pulp capping with mineral trioxide aggregate or calcium hydroxide: 2-to 6-year follow-up. *Clinical oral investigations*, *21*(1), 357-367.

Dhar, V., El-Karim, I., Coll, J. A., Fouad, A. F., O'Connell, A. C., Asgary, S., Bjørndal, L., Cehreli, Z. C., Crystal, Y. O., & Ekambaram, M. (2026). Consensus-Based Recommendations on Pulp Therapies in Primary and Permanent Teeth: IAPD Porto Forum. *International Journal of Paediatric Dentistry*.

Diogenes, A., & Henry, M. (2012). Pain pathways and mechanisms of the pulpo-dentin complex. *Seltzer and Bender's Dental Pulp, 2nd ed.; Hargreaves, KM, Goodis, HE, Tay, FR, Eds*, 159-184.

Duncan, H. F., Kirkevang, L. L., Peters, O. A., El-Karim, I., Krastl, G., Del Fabbro, M., Chong, B. S., Galler, K. M., Segura-Egea, J. J., & Kebschull, M. (2023). Treatment of pulpal and apical disease: the European Society of Endodontology (ESE) S3-level clinical practice guideline. *International endodontic journal*, *56*, 238-295.

El Karim, I. A., Cooper, P. R., About, I., Tomson, P. L., Lundy, F. T., & Duncan, H. F. (2021). Deciphering reparative processes in the inflamed dental pulp. *Frontiers in Dental Medicine*, *2*, 651219.

Endodontists, A. A. o. (2003). *Glossary of endodontic terms*. American Association of Endodontists.

Falakaloğlu, S., Özata, M. Y., & Plotino, G. (2023). Micro-shear bond strength of different calcium silicate materials to bulk-fill composite. *PeerJ*, *11*, e15183.

Galani, M., Tewari, S., Sangwan, P., Mittal, S., Kumar, V., & Duhan, J. (2017). Comparative evaluation of postoperative pain and success rate after pulpotomy and root canal treatment in cariously exposed mature permanent molars: a randomized controlled trial. *Journal of endodontics*, *43*(12), 1953-1962.

Haapasalo, M., Parhar, M., Huang, X., Wei, X., Lin, J., & Shen, Y. (2015). Clinical use of bioceramic materials. *Endodontic topics*, *32*(1), 97-117.

Innes, N., Frencken, J. E., Bjørndal, L., Maltz, M., Manton, D. J., Ricketts, D., Van Landuyt, K., Banerjee, A., Campus, G., & Doméjean, S. (2016). Managing carious lesions: consensus recommendations on terminology. *Advances in dental research*, *28*(2), 49-57.

Kahler, B., Taha, N., Lu, J., & Saoud, T. (2023). Vital pulp therapy for permanent teeth with diagnosis of irreversible pulpitis: biological basis and outcome. *Australian dental journal*, *68*, S110-S122.

Levin, L. G., Law, A. S., Holland, G., Abbott, P. V., & Roda, R. S. (2009). Identify and define all diagnostic terms for pulpal health and disease states. *Journal of endodontics*, *35*(12), 1645-1657.

Lin, L. M., Ricucci, D., Saoud, T. M., Sigurdsson, A., & Kahler, B. (2020). Vital pulp therapy of mature permanent teeth with irreversible pulpitis from the perspective of pulp biology. *Australian Endodontic Journal*, *46*(1), 154-166.

Linsuwanont, P., Wimonsutthikul, K., Pothimoke, U., & Santiwong, B. (2017). Treatment outcomes of mineral trioxide aggregate pulpotomy in vital permanent teeth with carious pulp exposure: the retrospective study. *Journal of endodontics*, *43*(2), 225-230.

Maltz, M., Garcia, R., Jardim, J., De Paula, L., Yamaguti, P., Moura, M., Garcia, F., Nascimento, C., Oliveira, A., & Mestrinho, H. (2012). Randomized trial of partial vs. stepwise caries removal: 3-year follow-up. *Journal of dental research*, *91*(11), 1026-1031.

Marques, M. S., Wesselink, P. R., & Shemesh, H. (2015). Outcome of direct pulp capping with mineral trioxide aggregate: a prospective study. *Journal of endodontics*, *41*(7), 1026-1031.

Matsuo, T., Nakanishi, T., Shimizu, H., & Ebisu, S. (1996). A clinical study of direct pulp capping applied to carious-exposed pulps. *Journal of endodontics*, *22*(10), 551-556.

McDonald, R. E., Avery, D. R., & Dean, J. A. (2010). Treatment of deep caries, vital pulp exposure, and pulpless teeth. *Mcdonald Avery's Dent Child Adolesc*, *9*, 343-365.

Mente, J., Petrovic, J., Gehrig, H., Rampf, S., Michel, A., Schürz, A., Pfefferle, T., Saure, D., & Erber, R. (2016). A prospective clinical pilot study on the level of matrix metalloproteinase-9 in dental pulpal blood as a marker for the state of inflammation in the pulp tissue. *Journal of endodontics*, *42*(2), 190-197.

Owatz, C. B., Khan, A. A., Schindler, W. G., Schwartz, S. A., Keiser, K., & Hargreaves, K. M. (2007). The incidence of mechanical allodynia in patients with irreversible pulpitis. *Journal of endodontics*, *33*(5), 552-556.

Parirokh, M., Torabinejad, M., & Dummer, P. (2018). Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview–part I: vital pulp therapy. *International endodontic journal*, *51*(2), 177-205.

Rechenberg, D., & Zehnder, M. (2020). Call for a review of diagnostic nomenclature and terminology used in endodontics. *International endodontic journal*, *53*(10), 1315-1317.

Ricucci, D., Loghin, S., & Siqueira Jr, J. F. (2014). Correlation between clinical and histologic pulp diagnoses. *Journal of endodontics*, *40*(12), 1932-1939.

Ricucci, D., & Siqueira Jr, J. F. (2020). Bacteriologic status of non-cavitated proximal enamel caries lesions. A histologic and histobacteriologic study. *Journal of Dentistry*, *100*, 103422.

Ricucci, D., Siqueira Jr, J. F., Li, Y., & Tay, F. R. (2019). Vital pulp therapy: histopathology and histobacteriology-based guidelines to treat teeth with deep caries and pulp exposure. *Journal of Dentistry*, *86*, 41-52.

Ricucci, D., Siqueira Jr, J. F., Rôças, I. N., Lipski, M., Shiban, A., & Tay, F. R. (2020). Pulp and dentine responses to selective caries excavation: a histological and histobacteriological human study. *Journal of Dentistry*, *100*, 103430.

Schwendicke, F., & Herbst, S. R. (2023). Health economic evaluation of endodontic therapies. *International endodontic journal*, *56*, 207-218.

Silva, E. J., Pinto, K. P., Riche, F. N., Carestiato, M. G., Martins, J. N., Duncan, H. F., Versiani, M. A., & De-Deus, G. (2025). A meta-analysis of calcium silicate-based cements and calcium hydroxide as promoters of hard tissue bridge formation. *International endodontic journal*, *58*(5), 685-714.

Simon, S., Perard, M., Zanini, M., Smith, A., Charpentier, E., Djole, S., & Lumley, P. (2013). Should pulp chamber pulpotomy be seen as a permanent treatment? Some preliminary thoughts. *International endodontic journal*, *46*(1), 79-87.

Soma, U., Sharma, R., Gupta, A., Abraham, D., Ahmad, L., & Neha, N. (2025). Clinical and Radiographic Outcomes Following Pulpotomy Using Biodentine in Carious Exposed Mature Permanent Teeth: A Systematic Review and Meta-analysis. *Journal of International Society of Preventive and Community Dentistry*, *15*(4), 313-322.

Souza, R. A., Gomes, S. C. N., Dantas, J. d. C. P., Silva-Sousa, Y. T., & Pécora, J. D. (2007). Importance of the diagnosis in the pulpotomy of immature permanent teeth. *Brazilian dental journal*, *18*(3), 244-247.

Taha, N. A., & Abdulkhader, S. Z. (2018). Full pulpotomy with biodentine in symptomatic young permanent teeth with carious exposure. *Journal of endodontics*, *44*(6), 932-937.

Taha, N. A., & Khazali, M. A. (2017). Partial pulpotomy in mature permanent teeth with clinical signs indicative of irreversible pulpitis: a randomized clinical trial. *Journal of endodontics*, *43*(9), 1417-1421.

Tan, S. Y., Yu, V. S. H., Lim, K. C., Tan, B. C. K., Neo, C. L. J., Shen, L., & Messer, H. H. (2020). Long-term pulpal and restorative outcomes of pulpotomy in mature permanent teeth. *Journal of endodontics*, *46*(3), 383-390.

Yoo, Y. J., Baek, S. H., Kum, K. Y., Shon, W. J., Woo, K. M., & Lee, W. (2016). Dynamic intratubular biomineralization following root canal obturation with pozzolan-based mineral trioxide aggregate sealer cement. *Scanning*, *38*(1), 50-56.

Zanini, M., Meyer, E., & Simon, S. (2017). Pulp inflammation diagnosis from clinical to inflammatory mediators: a systematic review. *Journal of endodontics*, *43*(7), 1033-1051.

Zehnder, M., Wegehaupt, F. J., & Attin, T. (2011). A first study on the usefulness of matrix metalloproteinase 9 from dentinal fluid to indicate pulp inflammation. *Journal of endodontics*, *37*(1), 17-20.