

**PATHOPHYSIOLOGY OF DENTAL PULP: CLINICAL FEATURES,
ETIOLOGY AND PATHOGENESIS**

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Abstract

Dental pulp is a specialized connective tissue located within the rigid confines of the dentin–enamel complex, responsible for vascular, neural, immune, and formative functions essential to tooth vitality. Pathological alterations in the pulp arise from a combination of microbial, mechanical, chemical, and thermal insults that induce a cascade of inflammatory, vascular, and neurogenic responses. This article provides a comprehensive overview of the clinical presentation, etiological determinants, and underlying pathophysiological mechanisms associated with pulp disease. A narrative review methodology was employed, analyzing contemporary scientific sources published between 2015–2024. The results reveal that pulp inflammation progresses through reversible and irreversible phases characterized by shifts in vascular permeability, cytokine expression, and extracellular matrix degradation, ultimately leading to necrosis if untreated. Clinically, pulp pathology manifests as thermal hypersensitivity, spontaneous pain, and altered response to vitality testing, corresponding to distinct histopathological stages. Understanding these mechanisms is crucial for early diagnosis and biologically based treatment approaches, including pulp preservation and regenerative therapies. The findings underscore the need for integrative diagnostic strategies that combine clinical evaluation, microcirculation assessment, and biomarker-based technologies. Future research should focus on immunomodulatory interventions and stem cell-based regenerative endodontics to preserve pulpal vitality.

Keywords

dental pulp, pulpitis, odontoblasts, inflammation, microcirculation, necrosis, dentin, cytokines, neurogenic pain, etiology.

Intradaction: Dental pulp is a specialized, vascularized, and innervated connective tissue enclosed within a rigid mineralized environment composed of enamel and dentin. Its primary functions include dentinogenesis through odontoblast activity, neurosensory transmission, immunological defense, and nutritional support for the dentin-pulp complex. Due to its unique anatomical confinement and limited collateral blood supply, the pulp is highly susceptible to pathological changes when subjected to external insults. Any disturbance to pulpal homeostasis, whether infectious or non-infectious, initiates a cascade of biological reactions that may lead to inflammation, ischemia, and ultimately necrosis if not addressed promptly. Understanding the pathophysiology of pulp disease is fundamental for accurate diagnosis, treatment planning, and preservation of tooth vitality.

The most common etiological factor in pulp pathology is dental caries, which remains a global burden. Carious lesions allow microbial entry, facilitating colonization by acidogenic and proteolytic bacteria such as *Streptococcus mutans*, *Lactobacillus* spp., and anaerobic gram-negative microorganisms. These pathogens produce toxins and metabolic byproducts that diffuse through dentinal tubules, triggering inflammatory mediators and activating both innate and adaptive immune responses. Mechanical trauma, restorative procedures, occlusal stress, orthodontic movement, and chemical irritation from dental materials also contribute to pulp injury independent of infection.

The clinical manifestation of pulp diseases varies according to the stage of inflammation. Reversible pulpitis generally presents with short, sharp pain induced by thermal stimuli, whereas irreversible pulpitis causes prolonged spontaneous pain due to sustained inflammation, increased intrapulpal pressure, and activation of nociceptive fibers. Advanced stages may progress to pulp necrosis, leading to periapical pathology, abscess formation, or chronic granulomatous lesions. Modern diagnostic approaches rely not only on symptomatic evaluation but also on technologies such as laser Doppler flowmetry, thermometric testing, cone-beam computed tomography (CBCT), and biomarker detection.

In recent decades, the paradigm of pulp treatment has shifted from complete removal toward biologically based therapies aimed at preserving vitality. Regenerative endodontics, mineral trioxide aggregate (MTA), calcium silicate-based biomaterials, and stem-cell-mediated tissue engineering represent emerging strategies. To utilize these approaches effectively, clinicians must understand the molecular pathways driving inflammation, neurovascular responses, apoptosis, and reparative dentinogenesis.

This study reviews the fundamental clinical features, etiology, and pathogenesis of dental pulp pathologies, synthesizing recent literature to provide an updated scientific perspective. The analysis emphasizes immune responses, cytokine regulation, vascular changes, and neurogenic mechanisms while correlating these with clinical stages and diagnostic criteria. A deeper understanding of these processes may improve therapeutic decision-making, enabling earlier intervention and enhanced long-term outcomes for dental patients.

MATERIALS AND METHODS: This study employed a narrative review methodology focusing on contemporary scientific literature related to dental pulp pathology, with emphasis on clinical presentation, etiological factors, and biological mechanisms underlying disease progression. Sources were collected from academic databases including PubMed, Scopus, Google Scholar, ScienceDirect, and Cochrane Library.

Search terms used individually or in combination included: “dental pulp inflammation,” “pulpitis pathogenesis,” “odontoblasts,” “pulp necrosis,” “neurogenic pain,” “pulp microcirculation,” “regenerative pulp therapy,” and “dentin-pulp complex.”

Inclusion criteria comprised peer-reviewed articles published between 2013 and 2024, focusing on original research, clinical trials, systematic reviews, and molecular studies. Articles addressing pulp regeneration, dental biomaterials, immune response pathways, and microbial etiology were prioritized. Exclusion criteria involved papers unrelated to pulp biology, studies on non-human species without translational relevance, low-quality anecdotal reports, and sources lacking credible methodology.

Data extraction involved categorizing findings into five primary domains:

- (1) etiological factors;
- (2) inflammatory response and cytokine signaling;
- (3) vascular and microcirculatory changes;
- (4) neural mechanisms and pain pathways;
- (5) progression to necrosis and repair potential.

No formal statistical analysis was conducted due to heterogeneity in study designs and outcomes. Instead, a qualitative synthesis approach was used to identify dominant themes, correlations, and emerging scientific consensus. Ethical approval was not required as the study did not involve human or animal subjects.

The purpose of this methodology was to develop a comprehensive, scientifically grounded review that integrates cellular, molecular, and clinical perspectives of pulp pathology. The structured synthesis enables comparative

interpretation of research findings and supports the development of evidence-based recommendations for clinical practice.

RESULTS: Analysis of the collected literature revealed that pathological changes in the dental pulp follow a distinct progression characterized by interrelated inflammatory, vascular, immune, and neural events. These processes vary depending on the intensity and duration of etiological stimuli. Findings were categorized into four major domains: (1) inflammatory mediator dynamics, (2) vascular and hemodynamic alterations, (3) neural sensitization and pain mechanisms, and (4) tissue breakdown leading to necrosis or reparative responses.

The first major finding was that inflammation begins prior to bacterial penetration into the pulp, occurring initially within dentinal tubules. Odontoblasts act as early immune sentinels by recognizing microbial components through pattern-recognition receptors such as Toll-like receptors (TLR-2, TLR-4). Activation of these receptors stimulates secretion of pro-inflammatory cytokines including interleukin-1 β (IL-1 β), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6), triggering chemotaxis of immune cells. Studies indicate that increased cytokine expression correlates with the severity of pulpitis and directly influences extracellular matrix degradation through matrix metalloproteinases (MMP-2, MMP-9). At early stages, inflammatory responses remain confined and reversible; however, persistent stimuli amplify immune signaling and promote irreversible tissue damage.

The second major finding was the crucial role of vascular changes and microcirculation impairment. Unlike other connective tissues, the pulp is enclosed within rigid dentin walls, restricting expansion. Vasodilation during inflammation increases pulpal pressure, reducing venous outflow and leading to localized ischemia. Histological examinations demonstrate that severe pulpitis is marked by engorged capillaries, endothelial disruption, and perivascular infiltration by neutrophils and macrophages. Prolonged ischemia contributes to apoptotic death of odontoblasts and replacement by inflammatory granulation tissue. Once ischemia reaches critical levels, necrosis becomes inevitable, especially in the pulp horn and coronal regions where vascular supply is most limited.

The third set of findings relates to neurogenic mechanisms responsible for pulpal pain. Sensory fibers in the pulp consist predominantly of myelinated A-delta fibers, responsible for sharp provoked pain, and unmyelinated C-fibers, responsible for dull, lingering spontaneous pain. Inflammation increases expression of neuropeptides such as calcitonin gene-related peptide (CGRP) and substance P, amplifying nociceptive signaling. Simultaneously, ion channels such as TRPV1 and Nav1.8 become upregulated, increasing neural excitability. This helps explain the

clinical shift from reversible thermal sensitivity to persistent spontaneous pain characteristic of irreversible pulpitis. The results also show that nerve sprouting and neurogenic inflammation further intensify vascular permeability, creating a feedback loop between neural and immune responses.

The fourth major finding concerns progression to necrosis and subsequent periapical disease. Necrotic pulp loses immune function, permitting proliferation of anaerobic bacteria, particularly *Prevotella*, *Porphyromonas*, and *Fusobacterium* species. These organisms and their endotoxins diffuse beyond the apical foramen, inducing periapical inflammation, cyst formation, and abscess development. Once necrosis occurs, regenerative capacity drastically decreases, leaving conventional root canal therapy as the primary treatment option unless biological regeneration is possible.

The fifth domain of results pertains to the regenerative and reparative potential of vital pulp tissue. When injury is moderate, living odontoblasts deposit reactionary dentin, while stem cells from the apical papilla and dental pulp stem cells may differentiate into odontoblast-like cells under the influence of growth factors such as TGF- β , BMP-2, and VEGF.

Contemporary findings highlight the role of bioceramic materials, including calcium silicate cements and MTA, which promote dentin bridge formation by releasing calcium ions and stimulating cell differentiation. These materials have been shown to significantly enhance clinical success rates in vital pulp therapy, particularly in young permanent teeth.

Overall, the results demonstrate that pulp pathology represents a dynamic continuum rather than discrete stages. Reversible changes can transition into irreversible damage depending on host immune competence, microbial virulence, and vascular resilience. Effective treatment strategies therefore require early diagnosis, control of inflammation, preservation of viable cells, and restoration of physiological microcirculation.

Key findings summarized:

Pathological Component	Primary Change	Clinical Correlation
Odontoblast response	Cytokine release, TLR activation	Early reversible pulpitis
Vascular changes	Increased pressure, ischemia	Persistent spontaneous pain
Neural changes	Upregulated nociceptive peptides	Irreversible pulpitis symptoms
Necrosis	Loss of vascular supply, anaerobic colonization	Periapical pathology

Regeneration Stem cell differentiation, dentinogenesis Recovery with vital therapies

DISCUSSION: The findings of this review highlight the complex and dynamic nature of dental pulp pathology, reinforcing the concept that pulp disease is not merely a linear process but a multidimensional biological cascade driven by host-microbe interactions, vascular regulation, and neuroimmune mechanisms. One of the most significant implications of these findings is the understanding that early inflammation, although typically reversible, can rapidly progress to irreversible states when compensatory mechanisms are overwhelmed. This progression emphasizes the need for timely intervention and diagnostic accuracy.

A major theme across studies is the pivotal defensive role of odontoblasts. Traditionally, odontoblasts were considered purely structural and dentin-forming cells; however, contemporary research identifies them as active immune participants capable of detecting pathogens and releasing pro-inflammatory mediators. Their strategic anatomical location along the pulp-dentin interface allows them to serve as biological gatekeepers against microbial invasion. This immunological role explains why superficial dentin lesions, even without pulpal exposure, may induce subclinical inflammation. Clinicians can leverage this understanding by selecting minimally invasive restorative approaches that preserve odontoblastic vitality rather than removing large dentin volumes unnecessarily.

Inflammatory cytokines such as IL-1 β and TNF- α were identified as key factors in matrix degradation and pain amplification. Increased cytokine levels are strongly correlated with irreversible pulpitis, suggesting potential diagnostic applications. Biomarker-based pulp tests—though not yet widely implemented—may advance diagnostic accuracy beyond traditional symptom-based assessments, which are often subjective and unreliable. Additionally, the interplay between immune and neural systems, especially the role of neuropeptides like CGRP, forms a positive feedback loop that accelerates vascular changes and increases pain sensitivity. This understanding provides a scientific basis for analgesic strategies that target neural pathways, rather than relying solely on anti-inflammatory drugs.

The vascular pathology of pulp disease remains a core determinant of clinical outcomes. Because of the rigid dentinal walls encasing pulp tissue, inflammation-induced vasodilation and plasma extravasation lead to elevated intrapulpal pressure, impairing venous drainage and ultimately triggering ischemia. This mechanism differentiates pulp inflammation from other soft tissue inflammations, where swelling can dissipate externally. Therapeutic interventions that reduce

pulpal pressure—such as partial pulpotomy or selective removal of infected dentin—may preserve vitality in cases where complete pulp extirpation would otherwise be considered.

Another significant implication is the recognition that pulp necrosis is not solely the endpoint of inflammation but a transition into new pathological states characterized by anaerobic microbial colonization and periapical tissue destruction. While conventional root canal therapy effectively removes necrotic tissue and disinfects canals, it does not restore biological function. As regenerative endodontics continues to advance, treatment paradigms may shift toward revascularization and stem cell-mediated pulp regeneration. Materials such as MTA, Biodentine, and other bioceramics have shown clinical success by creating favorable microenvironments for healing. Their ability to release bioactive ions and induce odontoblast-like cell differentiation offers a scientific rationale for their use over traditional calcium hydroxide in vital pulp therapy.

An important practical takeaway from these findings is the need for stratified treatment planning rather than binary classification into “reversible” and “irreversible” pulpitis. Emerging research suggests an intermediate category of “transitional pulpitis,” where partial inflammation can be reversed given appropriate biological intervention. In young permanent teeth, maintaining pulpal vitality is particularly critical due to reliance on continued root development and apical closure.

The role of host factors, including systemic inflammation, genetics, and comorbidities, also warrants attention. Individuals with diabetes, autoimmune disorders, smoking habits, or vitamin deficiencies exhibit altered immune responses that may accelerate pulpal deterioration and reduce healing capacity. Personalized dentistry that considers medical history and immunological profiles may therefore become essential.

Despite scientific advances, several limitations persist. Current diagnostic tools lack precision, most research is laboratory-based rather than clinical, and regenerative protocols remain unpredictable, particularly in necrotic teeth. Future studies should focus on developing standardized criteria for pulp inflammation severity, molecular diagnostic kits, and bioengineered scaffolds capable of supporting full neurovascular regeneration. Overall, integrating biological knowledge into clinical decision-making may transform pulp therapy from destructive intervention toward tissue preservation and regeneration, improving long-term oral health outcomes.

CONCLUSION: Dental pulp pathology represents a complex interplay of microbial invasion, immune activation, vascular disturbances, and neurogenic

mechanisms that collectively determine the clinical progression from reversible inflammation to irreversible pulpitis and necrosis. The findings of this review demonstrate that pulp disease should be understood as a dynamic continuum rather than a set of isolated stages, with odontoblasts playing a central role as immune regulators at the dentin-pulp interface. Early inflammation is characterized by cytokine release, neural sensitization, and microcirculatory changes, whereas advanced disease results in ischemia, tissue breakdown, and colonization by anaerobic bacteria leading to periapical pathology. Clinically, accurate diagnosis requires integration of symptomatic assessment, biological markers, and advanced imaging to differentiate stages of inflammation and guide treatment decisions. The therapeutic paradigm in endodontics is gradually shifting toward strategies that preserve or restore pulp vitality, including regenerative therapies and bioceramic biomaterials that promote dentinogenesis. Future research should focus on molecular diagnostics, stem-cell-based regeneration, and personalized treatment approaches based on patient-specific immune responses. Understanding the pathophysiology of pulp disease remains fundamental to improving patient outcomes and advancing biologically driven dental care.

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