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Narrative Review

Endodontic diagnosis under altered host immunity: Implications of immune suppression and immune dysregulation

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Abstract

Background: Endodontic diagnosis usually assumes that pain, tenderness, swelling, sensibility test responses, and radiographic change reflect the interaction between microbial irritation and host response. Under altered host immunity, this relationship becomes less predictable because disease activity and disease expression may no longer progress in parallel. Biologically important pulpal or periapical disease may therefore appear deceptively mild, whereas competing oral or systemic conditions may complicate localization and interpretation.

Objectives: To examine how altered host immunity changes the diagnostic expression of pulpal and periapical disease, distinguish immune suppression from immune dysregulation as biologically distinct states, and propose a practical clinical approach to diagnostic uncertainty in these patients.

Methods: A narrative review with structured integrative synthesis was conducted. PubMed/MEDLINE and Scopus were searched from database inception to April 2026, with reference-list screening of relevant reviews, clinical studies, and mechanistic papers. Search terms combined altered host immunity, immune suppression, immune dysregulation, autoimmune disease, immunomodulatory therapy, pulpitis, apical periodontitis, root canal treatment, endodontic diagnosis, pain, inflammation, imaging, and pulp sensibility. Sources were selected when they informed diagnostic expression, symptom interpretation, clinical test reliability, radiographic assessment, or practical decision-making. Evidence was grouped by immune suppression, immune dysregulation, and overlap states, then synthesized into a diagnostic framework.

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Results: Altered host immunity changed the diagnostic meaning of conventional endodontic findings in two broad directions. Immune suppression tended to attenuate inflammatory expression, with reduced pain, swelling, and delayed radiographic change, thereby increasing the risk of under-recognition. Immune dysregulation tended to reduce interpretive clarity through chronic inflammatory activity, mucosal disease, xerostomia, neuropathic overlap, and treatment-related oral change, thereby increasing the risk of misdirection or misdiagnosis. Conventional tests retained clinical value, but isolated interpretation became less secure. A practical five-step response was therefore proposed: define the immune context, classify the presentation pattern, interpret findings together, escalate imaging when needed, and recognize red flags early.

Conclusion: Altered host immunity does not invalidate conventional endodontic diagnosis. However, it requires more cautious and context-sensitive interpretation. Safer diagnosis depends on integration of medical history, tooth-specific examination, imaging, and reassessment over time, together with patience and empathy when uncertainty persists.

Key words: altered host immunity; apical periodontitis; endodontic diagnosis; immune dysregulation; immune suppression

Introduction

Endodontic diagnosis rests on the assumption that pain, tenderness, swelling, sensibility test responses, and radiographic change broadly reflect the interaction between microbial irritation and host response (Nair, 2004). When host immunity is altered, this relationship becomes less predictable because disease activity and disease expression may no longer move in parallel (Graves et al., 2011). A tooth with active pulpal or periapical disease may therefore present with reduced symptoms, delayed radiographic change, or competing signs from non-odontogenic sources.

Most reviews on medically compromised patients in endodontics discuss treatment precautions, antibiotic use, or outcome after treatment instead of diagnosis itself (Segura-Egea et al., 2015; Khalighinejad et al., 2016). This leaves an important gap because diagnosis determines whether infection is recognized early, whether mimicking conditions are excluded, and whether treatment is proportionate to the true disease burden. A review focused on diagnostic expression is therefore more clinically useful than a broad summary of management issues in systemic disease (Niazi & Bakhsh, 2022; Ye et al., 2023). Although recent studies and syntheses have examined apical periodontitis in autoimmune disease and in patients receiving immunosuppressive or immune modulatory therapy (do Nascimento et al., 2025), the literature remains focused mainly on prevalence, association, healing, and treatment-related effects rather than on how altered host immunity changes diagnostic interpretation itself.

The present review is built on the premise that altered host immunity affects diagnosis in two biologically distinct patterns. Immune suppression may blunt pain, swelling, and radiographic expression, which increases the risk of underdiagnosis. Conversely, immune dysregulation may amplify inflammatory tone, increase background oral symptoms, and complicate symptom localization, which increases the risk of overdiagnosis or misdiagnosis (Ideo et al., 2024; Mannocci et al., 2025). This bidirectional diagnostic distortion model gives the review a clearer conceptual identity than the usual umbrella category of "medically compromised patients".

Available evidence makes this distinction credible. Experimental work reported altered development of periradicular lesions in immunosuppressed

rats (Waterman et al., 1998). Clinical studies in hematopoietic stem cell transplantation show that endodontic infection may persist despite severe systemic compromise and therefore requires timely management before transplantation (Mota et al., 2025). By contrast, autoimmune disease introduces a different type of diagnostic difficulty because chronic inflammatory activation, oral mucosal disease, salivary dysfunction, and treatment-related effects interfere with the interpretation of classical endodontic findings and distort the usual clinical presentation (Guerrero-Gironés et al., 2021; Xu et al., 2024). This complexity has practical importance because immune-mediated oral disease is often recognized late or initially attributed to other causes (Petruzzi et al., 2023). Altered host immunity should therefore be considered from the outset of endodontic assessment because its effects may contribute to diagnostic uncertainty from the start.

This narrative review examines how altered host immunity changes the diagnostic expression of pulpal and periapical disease. It distinguishes immune suppression from immune dysregulation as biologically distinct states with different diagnostic consequences. The review analyzed the immunological basis of altered disease expression and examined how conventional diagnostic tools may become less reliable under altered host immunity. The review also develops a clinically oriented framework that helps clinicians interpret endodontic findings more accurately in patients with altered host immunity.

Methods

A narrative review with structured integrative synthesis was conducted. Literature was identified through targeted searches of PubMed/MEDLINE and Scopus, with reference list screening of relevant reviews, systematic reviews, clinical recommendation documents, and primary studies. Searches covered database inception to April 2026. Search terms were combined iteratively around three concept groups: altered immune status, endodontic disease, and diagnostic expression. Immune-related terms included immune suppression, immunosuppression, immune dysregulation, autoimmune disease, immunomodulation, biological therapy, disease-modifying antirheumatic drugs, chemotherapy, glucocorticoids, transplantation, neutropenia, rheumatoid arthritis, systemic lupus erythematosus, Sjögren disease, inflammatory bowel disease, type 1 diabetes mellitus, and multiple sclerosis. Endodontic and diagnostic terms included pulpitis, pulpal necrosis, apical periodontitis, periapical disease, root canal treatment, endodontic infection, dental pain, pulp sensibility, pulp vitality, radiographic diagnosis, cone beam computed tomography, swelling, and inflammation.

Publications were considered relevant when they informed how altered immunity changes the clinical, radiographic, or biological expression of pulpal and periapical disease. Experimental and non-endodontic immunology sources were retained only when they clarified mechanisms with direct diagnostic relevance. Priority was placed on literature with direct relevance to endodontic diagnosis, oral manifestations that could mimic or obscure odontogenic disease, immune mechanisms that could alter inflammatory expression, and clinical scenarios in which conventional diagnostic tests may become less reliable. Publications were excluded when they dealt mainly with systemic disease management, surgical or oncological treatment, drug efficacy, or general dental care without a clear connection to endodontic diagnostic interpretation.

The synthesis was organized in two stages. First, evidence was grouped according to immune suppression, immune dysregulation, and overlap states caused by combined disease activity and treatment. Second, findings were interpreted across diagnostic domains: symptom expression, clinical examination, pulp sensibility testing, radiographic interpretation, cross-sectional imaging, and referral or medical liaison thresholds. The final framework was developed by identifying recurring patterns of diagnostic distortion; no attempt was made to pool numerical outcomes

Altered host immunity and diagnostic distortion

Altered host immunity changes the diagnostic meaning of clinical and radiographic findings. Two response patterns are presented for the purpose of this review: immune suppression and immune dysregulation. Together, these patterns form a bidirectional diagnostic distortion model in which host response may shift away from the usual relationship between disease burden and diagnostic expression in two different directions (Figure 1). Immune suppression tends to attenuate inflammatory expression. Immune dysregulation tends to add competing symptom signals and source ambiguity. This distinction provides the framework for the subsections that follow (Isaacs & Burmester, 2020).

Immune suppression

Immune suppression refers to reduced host responsiveness caused by disease, treatment, or both. This state is encountered in patients receiving cytotoxic chemotherapy, glucocorticoids, transplant-related immunosuppression, broad-acting immunosuppressive drugs, or targeted immune modulation biologics (Hussain & Khan, 2022; Roberts & Fishman, 2022; Mustafa, 2023). From a diagnostic perspective, the relevant issue is not simply increased susceptibility to infection (Dropulic & Lederman, 2016). The more important problem is that an inflammatory reaction may appear less clinically expressive than expected (Handley & Hand, 2022). Pain may be attenuated, swelling may be limited, and radiographic change may lag behind biological activity. Experimental

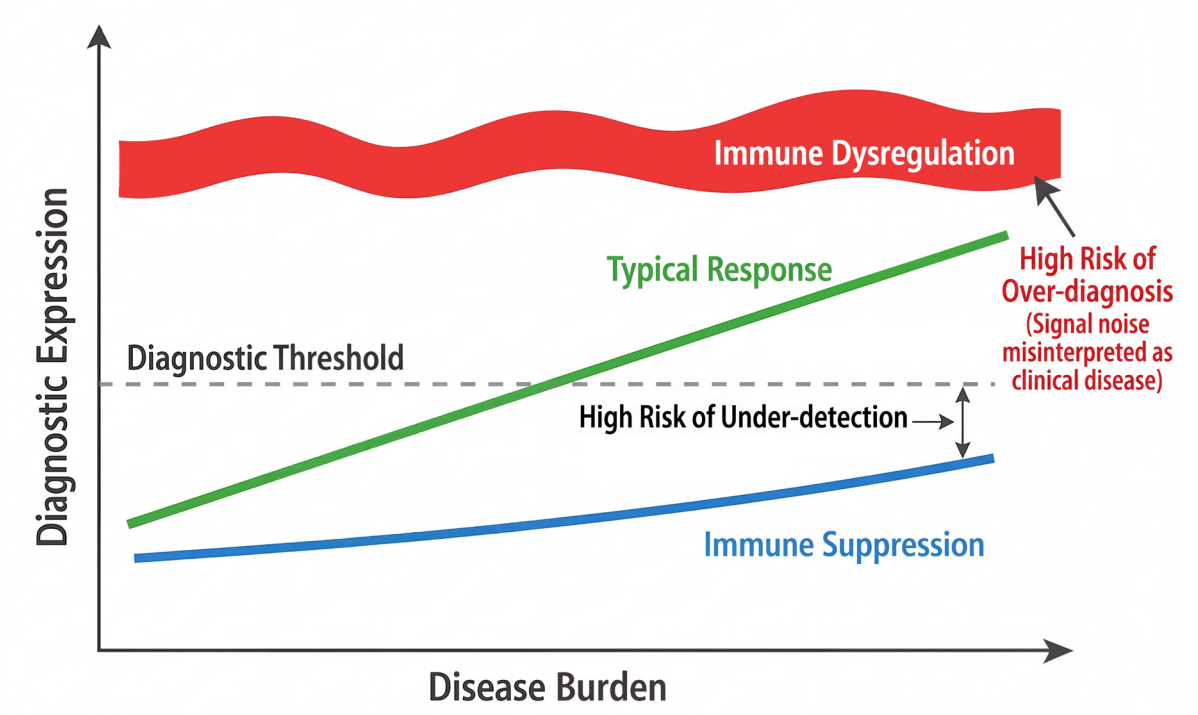


Fig. 1. Bidirectional diagnostic distortion model under altered host immunity. The horizontal axis represents underlying disease burden, and the vertical axis represents diagnostic expression, defined as the combined clinical and radiographic findings available to the clinician. The dashed horizontal line indicates the diagnostic threshold, namely the level of expression at which disease is likely to be recognized in routine assessment. In an immunologically typical host, diagnostic expression rises in broad proportion to disease burden. Under immune suppression, expression is attenuated and remains below the diagnostic threshold for longer, which increases the risk of under-detection or delayed recognition despite substantial disease burden. Under immune dysregulation, expression becomes amplified, unstable, or less specific, with earlier or repeated threshold crossing that may reflect competing inflammatory noise rather than proportionate odontogenic disease. The model illustrates how altered host immunity can distort diagnosis in two directions: towards under-recognition in immune suppression and towards over-interpretation or mis-localization in immune dysregulation.

work has shown that chronic systemic corticosteroid therapy altered the development of pulp necrosis and apical periodontitis, with modification of the inflammatory response and bone resorption pattern (do Nascimento et al., 2022). Cytotoxic therapy may also produce atypical pain presentations, including chemotherapy-induced odontalgia, which may mimic toothache in the absence of conventional odontogenic findings (Zadik et al., 2010). In practical terms, immune suppression increases the risk of underdiagnosis because mild or equivocal findings do not necessarily mean that the underlying disease is limited.

Immune dysregulation and overlap states

Immune dysregulation refers to altered or misdirected host activity instead of simple reduction in response. Malfunction of the immune system is characterized by breakdown in molecular control that results in chronic inflammation, autoimmunity, or immunodeficiency (Long et al., 2023). Autoimmune diseases are the main clinical models in this category. The diagnostic problem here is different. The issue is not chiefly reduced visibility of disease, but reduced clarity of interpretation. Background inflammatory activity, mucosal disease, dry mouth, structural breakdown, and medication-related effects may interfere with symptom localization and source attribution. Evidence from case-control studies suggests that patients with autoimmune disease have a higher prevalence of apical periodontitis than controls. However, this association varies across individual disease groups and medication categories, and may also be influenced by differences in overall dental disease burden (Allihaibi et al., 2023). Sjögren syndrome is especially relevant because dry mouth promotes root and cervical caries, multitooth involvement, and persistent oral discomfort. These symptoms make accurate localization of the odontogenic source more difficult (Donaldson et al., 2014; Khavandgar et al., 2024).

Overlap states refer to clinical situations in which immune dysregulation from the underlying autoimmune disease coexists with treatment-induced immunosuppression or immunomodulation. These states add further complexity because many patients with autoimmune disease also receive immunosuppressive or immunomodulatory therapy.

Table 1 summarizes the principal altered immune states relevant to endodontic diagnosis, their predominant immune patterns, the main sources of diagnostic distortion, and the immediate implications for clinical assessment.

Mechanistic basis of diagnostic distortion under altered host immunity

The mechanistic basis of diagnostic distortion lies in the fact that the clinical and radiographic signs used in endodontic diagnosis reflect host responses to infection rather than microbial burden alone (Graves et al., 2011). A comprehensive review of pulpal and periapical immunology is beyond the scope of this article. This section therefore focuses selectively on the host response pathways most relevant to altered diagnostic expression under immune suppression and immune dysregulation. Once bacterial products reach the pulp or periapical tissues, resident cells, vascular endothelium, and recruited inflammatory cells generate cytokines, chemokines, vasoactive mediators, and osteoclastogenic signals (Hahn & Liewehr, 2007; Pohl et al., 2024; Wen et al., 2024). Pain, tenderness, swelling, and radiographic radiolucency therefore represent downstream manifestations of host activity as opposed to direct measures of infectious severity. This distinction is central to the present review because altered host immunity modifies the intensity, timing, and tissue distribution of these host-mediated events and, in turn, changes diagnostic expression.

At the pulpal level, symptom expression arises largely from neurovascular and inflammatory changes within a confined tissue compartment (Kim & Dörscher-Kim, 1989). Vasodilatation, increased vascular permeability, release of inflammatory mediators, and neurogenic inflammation within the low-compliance pulp chamber contribute to

Table 1. Altered host immunity and its potential diagnostic effects in endodontics.

Condition or disease group	Dominant immune pattern	Characteristic oral features or confounders	Likely diagnostic distortion	Clinical implication
Chemotherapy-related neutropenia or myelosuppression	Reduced innate cellular response; transient or profound immune suppression	Oral mucositis, atypical dental pain, reduced overt inflammatory response	Under-expression of pain and swelling; possible misdirection when treatment-related pain mimics toothache	Absence of marked symptoms does not exclude clinically important infection; correlate history, examination, and imaging carefully
Hematopoietic stem cell transplantation and peri-transplant immunosuppression	Severe systemic immune suppression, often with neutropenia and broad treatment effects	Competing oral lesions, mucosal injury, persistent chronic odontogenic infection with limited acute signs	Under-expression with risk of sudden deterioration	Identify and stabilize endodontic disease early; maintain close communication with the hematology team
Chronic glucocorticoid therapy or broad immunosuppressive therapy	Broad suppression of inflammatory signaling and host defense	Reduced soft-tissue reaction, altered inflammatory tissue response	Under-expression of classical inflammatory signs	Do not rely on lack of swelling or limited tenderness as evidence of minor disease
Targeted biologics or selective immunomodulators	Selective pathway blockade or modulation rather than broad suppression	Disease-specific variation in inflammatory expression and healing behavior	Mixed expression; may not follow usual clinical expectations	Interpret findings in the context of both the underlying disease and the specific drug class
Rheumatoid arthritis	Immune dysregulation with cytokine-rich inflammatory activity	Background inflammatory burden, periodontal co-inflammation, altered pain interpretation	Over-expression or possible overestimation of local disease activity	Confirm that symptoms are tooth-specific before attributing them to pulpal or periapical disease
Systemic lupus erythematosus	Immune dysregulation with multisystem inflammatory and mucosal involvement	Oral ulceration, mucosal pain, secondary Sjögren overlap, non-odontogenic oral symptoms	Misdirection and symptom overlap	Exclude mucosal and systemic sources of pain before concluding that the tooth is the source
Sjögren syndrome	Autoimmune exocrine dysfunction with severe salivary hypofunction	Root and cervical caries, multiple heavily restored teeth, burning symptoms, candidal tendency, poor localization	Misdirection and multitooth ambiguity	Assess saliva-related disease burden and examine more than one plausible culprit tooth
Type I diabetes	Autoimmunity with metabolic dysfunction	Higher apical periodontitis prevalence, impaired healing, vascular compromise	Mixed expression with potential under-recognition	Do not equate mild symptoms with mild disease
Inflammatory bowel disease	Chronic immune dysregulation, often combined with drug-mediated immune modification	Oral ulceration, diffuse oral discomfort, medication-related oral change	Mixed distortion with overlap between odontogenic and non-odontogenic symptoms	Interpret toothache within the wider oral and medical context rather than as an isolated sign
Multiple sclerosis	Immune dysregulation with treatment modification of host response	Neuropathic pain, xerostomia, altered sensation	Misdirection and localization difficulty	Exclude non-odontogenic pain before assigning tooth origin

Note. Apical periodontitis may be distorted through underexpression, overexpression, or misdirection of signs and symptoms. The table is intended as a clinical interpretation aid rather than a disease classification system.

nociceptor sensitization and pulpal pain (Yu & Abbott, 2018). The important diagnostic implication is that pulpal symptoms are generated through host signaling pathways rather than through microbial presence alone. Altered host immunity may therefore change the character, intensity, or clarity of pulpal pain even when tissue injury persists.

At the periapical level, the dominant biological process is osteoimmune regulation (Graves et al., 2011). Apical periodontitis reflects a balance between pro-osteoclastogenic and counter-regulatory pathways more than the simple presence or absence of inflammation (Wen et al., 2024). Experimental and translational studies identify receptor activator of nuclear factor kappa-B (NFκB) ligand and osteoprotegerin balance as a central determinant of lesion behavior. A high receptor activator of NFκB ligand to osteoprotegerin ratio is associated with active osteolysis, whereas a lower ratio is more consistent with lesion stability (Cavalla et al., 2021). Tumor necrosis factor, interleukin 1, interleukin 6, and interleukin 17 promote inflammatory bone resorption, whereas interleukin 10, transforming growth factor beta, and regulatory lymphocyte activity favor a more restrained tissue response (Graves et al., 2011; Cavalla et al., 2021). Radiographic change appears only after these pathways have already produced sufficient hard tissue breakdown. Radiographic expression therefore lags behind the underlying biological process even in immunologically typical patients.

Altered host immunity changes these pathways in different directions. Immune suppression modifies these pathways chiefly by widening the gap between biological activity and clinical visibility. Development of periradicular lesions was altered in immunosuppressed rats (Waterman et al., 1998). This finding indicates that lesion expression depends on host responsiveness as much as on microbial challenge. More recent work showed that chronic systemic corticosteroid therapy exacerbated the development of pulp necrosis and experimental apical periodontitis, with altered inflammatory response and bone resorption patterns (do Nascimento et al., 2022). Another animal study showed that pharmacological immunomodulation can also alter the course and tissue expression of established periapical inflammation. In a mouse model, azithromycin reduced periapical bone loss, promoted a more pro-resolving macrophage profile, and suppressed pathogen-stimulated NFκB activation and production of interleukin 1-alpha and tumor necrosis factor-alpha (Andrada et al., 2020). These findings reinforce the concept that periapical lesion size, inflammatory-cell pattern, and healing status are shaped by host-response pathways instead of microbial infection alone. Immune suppression should therefore not be understood simply as reduced inflammation. It may also alter lesion kinetics, tissue destruction, and repair.

Immune dysregulation creates a different type of distortion. Here, the host response is not merely reduced, but misdirected or persistently activated. This state may intensify background cytokine activity, alter mucosal integrity, increase salivary dysfunction-related disease burden, and blur the boundary between odontogenic and non-odontogenic symptoms. The result is not a silent lesion, but a noisier diagnostic environment in which the source of symptoms becomes less clear.

In overlap states where autoimmune disease coexists with immunosuppressive or immunomodulatory therapy, both mechanisms may operate simultaneously. Objective inflammatory signs may be attenuated while competing symptom signals increase. Although this evidence comes from broader oral findings instead of apical periodontitis, recent case-control data indicate that biologic and disease-modifying antirheumatic drug therapy may alter the oral inflammatory environment in patients with rheumatic diseases (Hammad et al., 2024); this finding may also be relevant to endodontic interpretation. In some patients, autoimmune disease therapy may contribute to secondary immune deficiency, which reinforces the biological plausibility of mixed diagnostic distortion (Ballow et al., 2022; Labrosse & Haddad, 2023). This combined effect reduces the reliability of simple assumptions between symptom severity, tissue destruction, and disease origin.

The mechanisms discussed above are summarized in Figure 2, which illustrates how microbial irritation

produces host-mediated pulpal and periapical responses and how immune suppression or immune dysregulation may alter the final diagnostic expression.

A further concept of direct relevance to endodontics is that apical periodontitis does not remain biologically static over time. Periapical lesions move between more active and more stable states according to the balance between microbial stimulation and host regulation (Márton & Kiss, 2000; Cavalla et al., 2021). Regulatory T-cell pathways and other immunoregulatory mechanisms may restrain tissue destruction even when infection persists. Altered immune response, comorbid inflammation, dysbiosis, or therapeutic immune modification may disturb that balance and shift lesion behavior again (Fan et al., 2023; Pucinelli et al., 2025). The clinician therefore does not examine a fixed lesion, but a lesion captured at one point along an evolving host response continuum. Altered host immunity changes where that lesion lies on that continuum and how clearly it declares itself clinically.

Taken together, these mechanisms explain why altered host immunity modifies diagnosis at more than one level. It affects pain generation, inflammatory tissue response, osteoclast-mediated bone loss, radiographic detectability, and the balance between lesion activity and stability. The clinical signs used in endodontic diagnosis are therefore best understood as host-shaped outputs instead of direct readouts of microbial burden.

Diagnostic challenges in immune suppression

The most relevant diagnostic problem in immunosuppressed patients is poor agreement between biological severity and clinical expression.

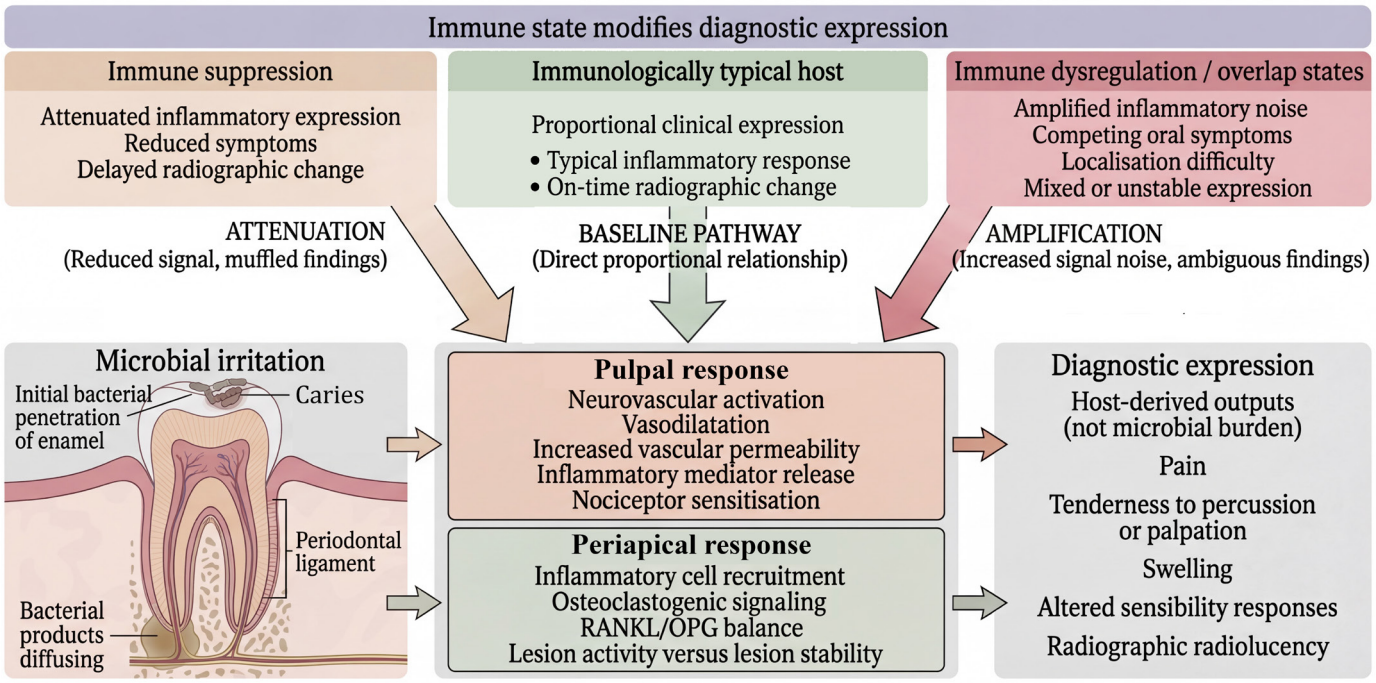


Fig. 2. Immune state modifies diagnostic expression in endodontic diseases. Microbial irritation initiates pulpal and periapical host responses that generate the clinical and radiographic findings used in endodontic diagnosis. In an immunologically typical host, diagnostic expression remains broadly proportional to underlying disease activity. Immune suppression attenuates this expression, with reduced symptoms and delayed radiographic change. In contrast, immune dysregulation or overlap states amplify or destabilize it through inflammatory noise, competing oral symptoms, and localization difficulty. Pain, tenderness, swelling, altered sensibility responses, and radiographic radiolucency therefore reflect host response patterns rather than microbial burden alone.can distort diagnosis in two directions: towards under-recognition in immune suppression and towards over-interpretation or mis-localization in immune dysregulation.

Severe odontogenic infection may produce limited pain, swelling, erythema, or suppuration because neutropenia and related immune deficits dampen the usual inflammatory response. A clinically mild presentation therefore does not reliably indicate limited disease (Parisi & Glick, 2003; Duduveche et al., 2026).

The first diagnostic challenge is reduced visibility of the local disease. In neutropenic patients, oral infection may progress despite minimal outward inflammation (Duduveche et al., 2026). Oral ulceration, periodontal inflammation, mucosal barrier injury, and untreated odontogenic foci have all been linked to infectious complications during myelosuppressive therapy or transplantation-related care (Raber-Durlacher et al., 2013; Nishi et al., 2022). Mild tenderness, limited swelling, or non-specific discomfort therefore require cautious interpretation in immunocompromised patients.

Glucocorticoid therapy provides a clear example of reduced diagnostic sensitivity in pulpal and periapical diseases. Glucocorticoids act on gene transcription and inhibit cyclooxygenase activity, leukotrienes, and cytokines (Lim et al., 2014; Cain & Cidlowski, 2017). They also suppress inflammatory mediators such as prostaglandin E2, bradykinin, and interleukin 8 in irreversible pulpitis (Hargreaves & Costello, 1990; Isett et al., 2003). Regular glucocorticoid use may therefore dampen spontaneous pain and reduce the conspicuity of symptom-based findings. Pulpal necrosis or periapical disease may appear less active than the underlying pathology justifies. For that reason, a seemingly mild presentation in a patient taking long-term glucocorticoids requires greater reliance on history, examination, and imaging than on pain intensity alone.

The second diagnostic challenge is poor localization, especially in patients receiving myelosuppressive chemotherapy. Mucositis, hyposalivation, oral ulceration, candidiasis, and treatment-related discomfort may coexist with odontogenic infection and blur the source of symptoms (Zecha et al., 2019; Duduveche et al., 2026). Chemotherapeutic regimens containing agents such as cyclophosphamide, vincristine, or methotrexate may induce neutropenia and oral mucositis (Zecha et al., 2022), thereby weakening mucosal barriers and reducing the host capacity to confine infection to a discrete periapical site. Under these conditions, odontogenic infection may present with vague dental pain, mucosal soreness, throat discomfort, or fever. For endodontic diagnosis, apparently minor dental symptoms during myelosuppressive therapy require cautious interpretation because infection may be less well contained. Instead of a well-defined abscess, odontogenic infections in patients receiving myelosuppressive medication may manifest as diffuse cellulitis (Carey & Dall, 1990). Spread beyond the immediate tooth-bearing tissues may occur before obvious local findings emerge.

These features lower the threshold for imaging. Whereas conventional dental radiographs are useful for source identification, cross-sectional imaging becomes more important when symptoms appear mild relative to risk, when spread of infection beyond the alveolar process is suspected, or when the medical context raises concern. Computed tomography and cone beam computed tomography continue to be the standard imaging methods in acute odontogenic infection because of availability and speed. These imaging methods are especially useful for rapid assessment of deep extension, airway obstruction, and thoracic spread (Rautaporras et al., 2023). Magnetic resonance imaging (MRI) may offer important added value where it is readily available because of its ability to detect edematous changes in soft tissues (Flügge et al., 2023; Greiser et al., 2024; Vaddi et al., 2025). This is because emergency neck MRI detects odontogenic abscesses with high accuracy and also identifies the causative tooth with good reliability. In the 106-patient cohort analysed by Heikkinen and colleagues, MRI showed sensitivity, specificity, and accuracy of 0.95, 0.84, and 0.92 for abscess detection. Mediastinal oedema was identified as the strongest imaging predictor of the need for extraoral surgery (Heikkinen et al., 2023).

The third diagnostic challenge is rapid extension once local containment fails. Severe odontogenic infections may spread from a seemingly limited

dental focus into deeper fascial spaces of the head and neck, Associated risks include airway obstruction, descending necrotizing mediastinitis, sepsis, and cervical necrotizing fasciitis (Neal & Schlieve, 2022; Rautaporras et al., 2023). Any medical condition that causes immune suppression allows odontogenic infection to disseminate more rapidly (Neal & Schlieve, 2022). Among these conditions, type II diabetes deserves particular attention because of its high prevalence, its deleterious effects on immune function, and its association with more extensive spread of odontogenic infection (Alexander et al., 2024). Uncontrolled type II diabetes is associated with microvascular and macrovascular change, impaired cytokine production, and impaired leukocyte recruitment and function (Berbudi et al., 2020; Li et al., 2023). In patients with severe odontogenic infections, higher blood glucose levels have also been associated with greater severity of infection (Hammad et al., 2022).

Taken together, immune suppression complicates endodontic diagnosis through three linked mechanisms: reduced visibility of local disease, poorer localization of symptoms, and more rapid extension once infection escapes local containment. The practical consequence is that mild symptoms or limited local signs cannot be taken as reassuring in these patients. Clinical judgement depends heavily on medical context, targeted imaging, and earlier recognition of biologically important disease. A clinical case is included to illustrate how chemotherapy-related immune suppression may mute the usual clinical expression of pulpal-periapical infection and make biologically important disease appear deceptively mild (Case 1, Supplementary Information). Written informed patient consent was obtained for presentation of this anonymized case for educational purposes.

Diagnostic challenges in immune dysregulation

Immune dysregulation is the broader category relevant to this section, and autoimmune diseases are the predominant clinical conditions within it. Autoimmune diseases are a specific group of disorders in which loss of immune self-tolerance causes the adaptive immune system to react against the body's own tissues, with chronic inflammation, tissue injury, and organ dysfunction as the result (Wang et al., 2015). Autoimmune diseases are therefore the main clinical models used in this review. Although immune dysregulation also extends beyond autoimmunity into other forms of immune malfunction such as immunodeficiency, allergy, and hypersensitivity, these conditions are beyond the present scope. Contemporary reviews describe autoimmune diseases as multifactorial diseases that arise through interaction between genetic susceptibility, environmental triggers, and immune dysregulation (Pisetsky, 2023; Song et al., 2024; Song et al., 2025).

Autoimmune diseases are clinically heterogeneous. The A-Z list maintained by the Global Autoimmune Institute currently contains 137 entries (https://www.autoimmuneinstitute.org/resources/autoimmune-diseases-list/; accessed April 28, 2026). It illustrates the breadth of autoimmune conditions that may alter oral findings, symptom interpretation, and diagnostic confidence in endodontic practice. A comprehensive disease-by-disease account is therefore neither practical nor necessary. The present review instead concentrates on autoimmune diseases that are most relevant to endodontic diagnosis and most illustrative of the ways in which autoimmunity may distort symptom interpretation and source attribution. Rheumatoid arthritis, systemic lupus erythematosus, Sjögren disease, inflammatory bowel disease, type 1 diabetes, and multiple sclerosis are well-established examples within this category (Saccucci et al., 2018; Karataş et al., 2020; Limeira et al., 2020; Poyato-Borrego et al., 2020; Al Johani et al., 2023).

The diagnostic challenge in autoimmune disease is not usually the simple attenuation of inflammatory expression seen in broad immunosuppression. Instead, the problem more often lies in altered interpretive clarity. Chronic inflammatory activity, mucosal disease, salivary dysfunction, background pain, structural dental breakdown, and treatment-related modification of host response may all interfere with localization of the odontogenic source. In this context, classical endodontic findings may still occur, but their diagnostic meaning becomes less straightforward (Guerrero-Gironés et al., 2021). This is especially relevant in autoimmune diseases affecting connective tissue or exocrine

function, in which oral symptoms may be persistent, overlapping, or only partly odontogenic in origin (Song et al., 2025).

The discussion that follows focuses exclusively on classic autoimmune diseases. However, the diagnostic framework also extends into autoinflammatory diseases when similar mechanisms distort endodontic interpretation (Parentelli et al., 2025). Both of these disease categories are considered inborn errors of immunity. Unlike autoimmune diseases that involve the adaptive immunity system (autoreactive T and B cells), autoinflammatory diseases are caused by activation of innate immune cells that result in dysregulated secretion of pro-inflammatory cytokines, chronic inflammation, and damage to healthy host tissue (Sabat et al., 2025). A supplementary case of hidradenitis suppurativa is included as a boundary example to illustrate how diagnostic distortion may likewise occur when an autoinflammatory condition and immune targeted treatment obscure identification of the true tooth-specific source (Case 2, Supplementary Information). Written informed patient consent was obtained for presentation of this anonymized case for educational purposes.

Predominantly disease-specific and treatment-mediated diagnostic models

Rheumatoid arthritis currently provides the clearest autoimmune model for a disease-specific link with pulpal-periapical pathology (Karataş et al., 2020). A recent systematic review found that three of five human studies reported a significant association and concluded that rheumatoid arthritis may be associated with pulpal-periapical pathology (Karataş et al., 2023). This is biologically plausible because rheumatoid arthritis and apical periodontitis share inflammatory mediators involved in tissue injury and bone resorption; rheumatoid autoimmunity may arise initially at mucosal sites such as the periodontium before systemic expression becomes established (Di Matteo et al., 2023; Karataş et al., 2023). Experimental evidence also suggests that rheumatoid immune dysregulation may prolong pulpitis and apical periodontitis instead of simply intensifying destruction (Yamazaki et al., 2023).

The main diagnostic problem is a noisier interpretation. Oral manifestations of rheumatoid arthritis and its associated treatment such as periodontal inflammation, temporomandibular symptoms, dry mouth, oral mucosal lesions, and candidiasis may all coexist and reduce confidence in localization of a tooth-specific source (Hammad et al., 2024). In patients with rheumatoid arthritis, symptoms should therefore be interpreted cautiously when discomfort attributed to periodontal disease, xerostomia, mucosal findings, and temporomandibular dysfunction are also present.

Systemic lupus erythematosus creates a different diagnostic problem from rheumatoid arthritis. Direct pulpal-periapical evidence for systemic lupus erythematosus is limited. A systematic review of pulpal periapical pathology and autoimmune disease found evidence for rheumatoid arthritis, type 1 diabetes mellitus, and inflammatory bowel disease, but not robust lupus-specific evidence (Guerrero-Gironés et al., 2021). Hence, difficulty in endodontic diagnosis arises more from treatment-related alteration of oral findings than from the disease itself (Dai et al., 2025). Glucocorticoids attenuate innate and adaptive immune responses (Cain & Cidlowski, 2017). Hydroxychloroquine suppresses toll-like receptor signaling and cytokine production (Al-Hamadani et al., 2025). Immunosuppressive agents such as mycophenolate mofetil, azathioprine, and cyclophosphamide inhibit lymphocyte proliferation (Hussain & Khan, 2022). Biologic agents such as belimumab and rituximab modify B cell pathways (Wise & Stohl, 2020). These treatment effects may blunt inflammatory signs, alter infection susceptibility, and add competing oral findings. Nevertheless, oral lupus symptoms such as oral ulcers, hyposalivation, glossodynia, cheilitis, and secondary Sjögren syndrome (De Rossi & Glick, 1998; García-Ríos et al., 2022, Hu et al., 2025) may coexist with treatment-related immune modification and further reduce confidence in localization of the true odontogenic source.

Sjögren disease as an overlap model

Sjögren disease (SjD), formerly known as Sjögren's syndrome (Ramos-Casal et al. 2025), is a serious autoimmune disease that affects glandular tissues (Baldini et al., 2024). In SjD, immune mediated injury to the salivary and lacrimal glands is induced by the interactions between B cells and T cells, with lymphocytic infiltration and B cell hyperactivity contributing to progressive glandular damage (Meng et al. 2024). These immune processes target

gland associated antigens, sustain local inflammation, and impair secretory function. The result is reduced salivary and tear production, which presents clinically as decreased salivary flow and keratoconjunctivitis sicca, the cardinal manifestations of the disease (Cox et al., 2026). Sjögren disease is a useful illustration of an overlap state in which the underlying autoimmune disease and its treatment can both distort endodontic diagnosis, albeit through different mechanisms.

At the disease level, SjD is characterized by autoimmune exocrine gland dysfunction with marked salivary hypofunction (Matthews et al., 2008). This persistently reduced salivary flow is subjectively manifested as xerostomia that compromises lubrication, buffering, antimicrobial activity, and enamel remineralization (Rihab et al., 2023). These dysfunctions promote rapid multifocal root and cervical caries, recurrent restorative failure, candidal overgrowth, burning symptoms, dysphagia, and progressive tooth loss (Liu et al., 2025). Patients with Sjögren disease also show increased oral disease burden, including higher rates of caries, pulpitis, oral ulceration, stomatitis, and tooth loss (Liu et al., 2025). In endodontic terms, the main problem is reduced confidence in source attribution. This is because several teeth may appear clinically plausible at the same time while mucosal discomfort, candidiasis, or burning symptoms further complicate localization (Al-Hashimi, 2001).

The overlap state becomes more diagnostically difficult once treatment is initiated. Saliva directed agents such as pilocarpine and cevimeline may increase salivary output and partly reduce dryness related discomfort. However, these agents may not eliminate the underlying pattern of multitooth risk and may change symptom intensity over time (Muszyński et al., 2025). Systemic therapy can further distort endodontic interpretation. Drugs used in SjD include glucocorticoids, hydroxychloroquine, methotrexate, azathioprine, cyclosporine, interferon alpha, rituximab, and other immunomodulatory biologics (Ramos-Casals et al., 2020; Baldini et al. 2024). These drugs can modify inflammatory signaling, alter infection susceptibility, and contribute to oral candidiasis, stomatitis, allergic mucositis, or other treatment-related oral discomfort (Mathews et al., 2008). As a result, treatment may both mute the expected inflammatory expression of odontogenic disease and introduce competing oral symptoms that weaken the anticipated relationship between symptom intensity and endodontic severity. Endodontic diagnosis for patients with SjD should therefore account not only for saliva-related disease burden, but also for medication history and treatment-related oral change before concluding that pain is odontogenic in origin.

Other common autoimmune diseases

Type 1 diabetes mellitus, inflammatory bowel disease, and multiple sclerosis are included here not because they provide disease specific diagnostic models as clear as rheumatoid arthritis. They are included because they extend the clinical relevance of the framework to other autoimmune conditions that may alter endodontic interpretation through different mechanisms. For these diseases, the available literature is focused mainly on the prevalence of apical periodontitis, root canal treatment, lesion burden, or healing after treatment rather than on how the disease itself or its medications directly alter chairside endodontic diagnosis (Limeira et al., 2020; Piras et al., 2017; Poyato-Borrego et al., 2020; Cotti et al., 2018; Al Johani et al., 2023). Their value in this review is therefore interpretive instead of exemplary. They show that autoimmune diseases do not distort diagnosis in one uniform direction. The dominant mechanism may differ according to whether disease activity, metabolic dysfunction, oral manifestations, neurological overlap, or treatment related immune modification is most influential in the individual patient.

Type 1 diabetes mellitus is autoimmune in origin (Jacobsen & Schatz, 2026), but its endodontic diagnostic behavior is mixed instead of purely inflammatory. In a cross-sectional paired study, root canal treatment, apical periodontitis, and root canal treatment associated with apical periodontitis were all more prevalent in individuals with type 1 diabetes mellitus than in controls. Apical periodontitis was

associated with glycemic control, whereas root canal treatment was associated with disease duration (Limeira et al., 2020). Earlier work in insulin-dependent diabetes also suggested that a subgroup of patients with longer disease duration may develop more periapical lesions and show less favorable periapical status after root canal treatment (Falk et al., 1989). These studies do not establish a distinctive disease specific diagnostic phenotype. However, they indicate that metabolic control, duration of disease, vascular compromise, and impaired host defense can modify lesion behavior and healing potential (Limeira et al., 2020; Falk et al., 1989). Type 1 diabetes mellitus is therefore best understood as an autoimmune disease in which endodontic expression may shift toward a mixed pattern, in which autoimmune pathogenesis coexists with metabolic dysfunction that can weaken infection control and tissue repair. In practical terms, apparently limited symptoms should not be assumed to indicate limited pulpal or periapical disease when glycemic control is poor.

Inflammatory bowel disease includes the two main entities, Crohn's disease and ulcerative colitis (Tavakoli et al., 2021). Both are relevant to endodontic diagnosis even though the present literature is weighed more toward prevalence of apical periodontitis, root canal treatment, and healing than towards direct chairside diagnostic effects (Guerrero-Gironés et al., 2021). Crohn's disease may involve any part of the gastrointestinal tract, most often the terminal ileum. It is characterized by transmural inflammation, fissuring ulceration, and granulomatous change. In contrast, ulcerative colitis is confined to the colon and rectum and is limited largely to the mucosa and submucosa (Poyato-Borrego et al., 2020; Song et al., 2025). Both conditions are associated with chronic immune imbalance and extraintestinal manifestations, including oral involvement. However, they have not yet demonstrated a clearly defined disease-specific pulpal-periapical phenotype. Case control studies have nevertheless reported a higher prevalence of apical periodontitis or radiolucent periapical lesions in patients with inflammatory bowel disease than in controls (Piras et al., 2017; Poyato-Borrego et al., 2020). From a diagnostic perspective, Crohn's disease and ulcerative colitis are therefore best understood as conditions that broaden the inflammatory and oral background against which endodontic findings are interpreted. Medication may further modify healing and lesion behavior, as suggested by the more rapid post-treatment healing reported in patients receiving anti-tumor necrosis factor-α therapy (Cotti et al., 2018).

Multiple sclerosis is also relevant, but for a different reason. Here, the strongest literature addresses oral manifestations, symptom overlap, and dental management instead of pulpal or periapical pathology. Multiple sclerosis may present with trigeminal neuralgia, facial pain, paranesthesia, dysarthria, dysphagia, temporomandibular symptoms, xerostomia, periodontal disease, and manual dexterity problems that impair oral hygiene and increase background oral disease burden (Patel et al., 2022; Al Johani et al., 2023). There is no cure for multiple sclerosis. Treatment typically focuses on speeding recovery from attacks, reducing relapses, slowing the progression of the disease and managing symptoms. Treatment for multiple sclerosis acute attacks commonly involves high dose corticosteroids. Longer-term disease-modifying management may include injection or infusion treatment involving interferon β, glatiramer acetate, B cell-depleting monoclonal antibodies (e.g. ofatumumab, natalizumab, ocrelizumab, ublituximab, alemtuzumab), as well as oral treatment such as teriflunomide, fumaric acid derivatives, sphingosine 1-phosphate receptor modulators (e.g. fingolimod, siponimod, ozanimod), and cladribine (Saleem et al., 2019; Callegari et al., 2021; Lee & Chan, 2024). All of these medications have implications for oral health, infection risk, and drug interactions relevant to dental care. Multiple sclerosis is included in the review because neurological pain overlap, altered sensation, xerostomia, and treatment-related oral effects may weaken localization and increase the risk of attributing pain to the wrong source. In this setting, excluding neuropathic and non-odontogenic causes of orofacial pain is necessary prior to concluding that the tooth is responsible.

The 137 autoimmune diseases currently listed

by the Global Autoimmune Institute are unlikely to conform to a single diagnostic pattern. The six conditions discussed in this review should therefore be read as illustrative anchors rather than a comprehensive disease map. Some autoimmune diseases may behave more like rheumatoid arthritis, in which disease-related inflammatory activity predominates. Others may behave more like systemic lupus erythematosus, in which treatment-related immune modification is more important. Many will fall between these poles and behave as overlap states, with combined contributions from the disease itself, associated oral manifestations, and the drugs used to control the disorder. The practical implication is that autoimmune disease should not be expected to produce one fixed endodontic phenotype. Diagnosis should instead be interpreted according to the dominant source of distortion in the individual patient: disease-predominant, treatment-predominant, or mixed.

Diagnostic tools and their limitations under altered host immunity

Pain history, clinical examination, sensibility testing, and radiographic assessment still form the basis of diagnosis. However, each of these methods depends as much on host response as on microbial burden. Their diagnostic value therefore becomes less secure when immune suppression, immune dysregulation, or overlap states alter the usual relationship between disease activity and disease expression. Mild findings may conceal biologically important disease, whereas symptom-rich presentations may still fail to identify the true odontogenic source. Diagnostic judgement in these settings depends less on any single sign and more on concordance across history, examination, imaging, and medical context.

Clinical tests and symptom interpretation

Altered host immunity does not render conventional endodontic tests obsolete. Clinical tests remain central to endodontic diagnosis but altered host immunity makes symptom interpretation less reliable. In immune suppression, pain, swelling, and tenderness may be reduced despite pulpal or periapical disease (Parisi & Glick, 2003; Cain & Cidlowski, 2017). In immune dysregulation, symptoms may be present but less specific because mucosal disease, hyposalivation, candidiasis, periodontal inflammation, temporomandibular symptoms, neuropathic pain, and treatment related discomfort can all complicate localization (Guerrero-Gironés et al., 2021; Al Johani et al., 2023; Hammad et al., 2024;).

Pulp sensibility tests also require caution. Thermal and electric tests assess neural response instead of pulpal blood supply, so their findings are indirect (Yu & Abbott, 2018). The same applies to percussion, palpation, and periodontal probing. These tests are still useful, but they should be interpreted within the overall clinical pattern rather than in isolation.

Radiographical assessment and cross-sectional imaging

Radiographic assessment becomes more important when clinical expression is unreliable. Conventional periapical radiographs are still essential, but radiographic change may lag behind underlying disease activity (Cavalla et al., 2021; Wen et al., 2024). In patients with altered host immunity, absence of an obvious radiolucency does not reliably exclude important disease.

Cone beam computed tomography may help when clinical and radiographic findings are discordant, or when more than one tooth appears plausible. Medical cross-sectional imaging becomes more important when spread beyond the alveolar process is suspected, or when severe infection is a concern despite limited local signs. Computed tomography remains central in acute odontogenic infection, while MRI may add value for soft tissue extension and abscess detection (Rautaporras et al., 2023; Heikkinen et al., 2023).

Figure 3 translates the clinical principles discussed in this section into a stepwise diagnostic pathway for patients presenting with suspected pulpal or periapical disease under altered host immunity. It summarizes how immune suppression, immune

dysregulation, and overlap states can modify symptom expression, influence interpretation of findings, and indicate when escalation, medical liaison, or urgent intervention is required. Diagnostic judgement must therefore rely on the integration of history, examination, imaging, and medical context more than in immunologically typical patients. These limitations provide the rationale for a more explicit practical framework for clinical use.

How the clinician should respond to diagnostic uncertainty

Altered host immunity changes interpretation of endodontic findings. In clinical practice, response to this uncertainty may be organized in five steps: 1) define the immune context, 2) classify the presentation pattern, 3) interpret findings together,

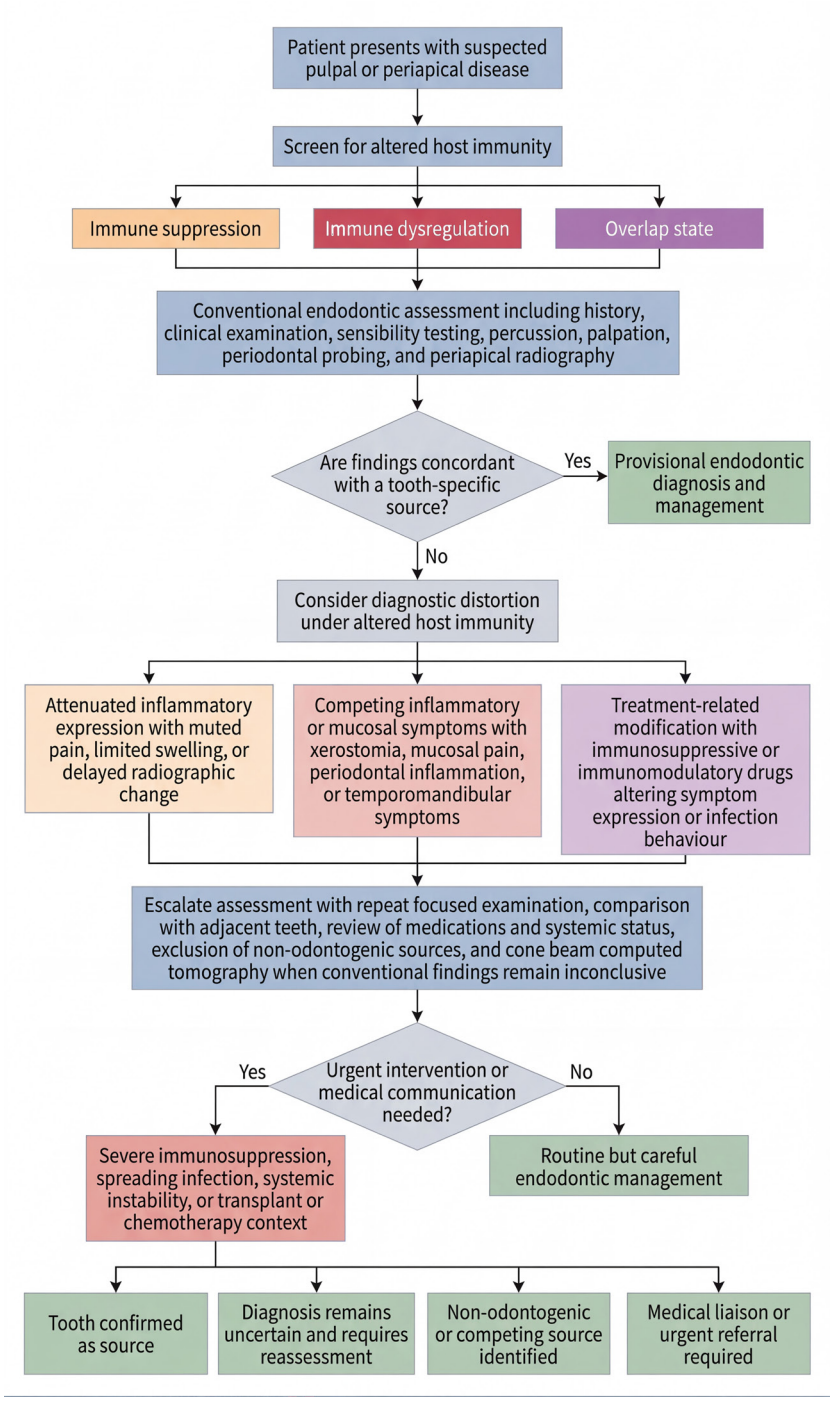


Fig. 3. Diagnostic algorithm for endodontic evaluation under altered host immunity. Stepwise clinical pathway for patients presenting with suspected pulpal or periapical disease. After screening for altered host immunity, the pathway distinguishes immune suppression, immune dysregulation, and overlap states before proceeding to conventional endodontic assessment. Concordant findings permit provisional endodontic diagnosis and management, whereas discordant findings prompt consideration of diagnostic distortion related to altered inflammatory expression, competing mucosal or periodontal symptoms, or treatment-related symptom modification. The algorithm then directs escalation through repeat focused examination, comparison with adjacent teeth, review of medications and systemic status, exclusion of non-odontogenic sources, and cone beam computed tomography when conventional findings remain inconclusive. Final branches identify situations requiring urgent intervention or medical communication and distinguish confirmed odontogenic disease from uncertain, competing, or non-odontogenic sources. Color coding indicates pathway function: blue, assessment steps; orange, immune suppression and attenuated inflammatory expression; red, immune dysregulation and high-risk escalation points; purple, overlap state or treatment-related modification; green, management or outcome endpoints; grey diamonds, decision nodes.

4) escalate imaging when needed, and 5) recognize red flags early (Yu & Abbott, 2018; Xu et al., 2024).

Define the immune context

The first step is to define the immune context before interpreting the dental findings. The clinician should identify whether the patient is most consistent with immune suppression, immune dysregulation, or an overlap state by reviewing the underlying diagnosis, current disease status if known, and recent or ongoing therapy. The latter includes the use of glucocorticoids, cytotoxic chemotherapy, biologics, disease-modifying antirheumatic drugs, and transplant-related immunosuppressants (Isaacs & Burmester, 2020; Roberts & Fishman, 2021; Xu et al., 2024). This distinction is clinically relevant because immune suppression raises concern for under-expression of pain, swelling, and radiographic change. Conversely, immune dysregulation raises concern for competing symptoms and reduced localization.

Classify the presentation pattern

The next step is to classify whether the presentation is under-expressed, misdirected, or concordant. An under-expressed pattern is present when symptoms and local signs appear milder than the medical context would suggest, as may occur in neutropenia, chemotherapy-related myelosuppression, or glucocorticoid use (Parisi & Glick, 2003; Zecha et al., 2019). A misdirected pattern is present when symptoms are prominent, but localization is uncertain because other oral or facial conditions may be contributing. Examples of those conditions include hyposalivation, candidiasis, mucosal disease, periodontal inflammation, temporomandibular symptoms, or neuropathic pain (Guerrero-Gironés et al., 2021; Al Johani et al., 2023; Hammad et al., 2024). A concordant pattern is present when the history, clinical findings, and imaging all indicate the same tooth and the same disease process.

Interpret findings together

Diagnosis should then be based on triangulation of findings instead of on one isolated result. History, sensibility tests, percussion, palpation, periodontal probing, restorability, caries status, and imaging should be interpreted together. This is because each finding reflects host response to some extent instead of microbial burden alone (Yu & Abbott, 2018; Cavalla et al., 2021; Wen et al., 2024). Under altered host immunity, lack of swelling does not exclude important disease, a weak sensibility response does not confirm vitality, and prominent pain does not by itself prove an odontogenic source when competing oral conditions are also plausible.

Escalate imaging when needed

Further imaging and reassessment should be considered earlier when the pattern is incomplete or discordant. Cone beam computed tomography may be useful when symptoms are not explained by conventional radiographs, when structural disease seems greater than what two-dimensional imaging suggests, or when more than one tooth appears plausible. Review over time may also be safer than premature irreversible root canal treatment when the findings do not align. When spread beyond the alveolar process is suspected, or when severe infection is a concern despite limited local signs, escalation should move beyond dental imaging alone. Computed tomography is indispensable for diagnosing acute odontogenic infection. Magnetic resonance imaging may add value for soft tissue extension and abscess detection (Heikkinen et al., 2023; Rautaporras et al., 2023).

Recognize red flags early

Some presentations should no longer be treated as routine endodontic diagnostic problems. Red flags include fever, rapidly progressive pain or swelling, diffuse cellulitis, trismus, dysphagia, airway concern, systemic deterioration, and persistent symptoms in a severely immunocompromised patient despite limited local findings (Neal & Schlieve, 2022; Rautaporras et al., 2023). In these settings, the biological risk may exceed the apparent local severity.

Early medical liaison is also warranted in patients

receiving active chemotherapy, transplant-related care, or complex immunosuppressive regimens. Communication with the treating medical team may clarify the degree of immune compromise, timing of therapy, hematological risk, and whether urgent dental intervention or closer monitoring is required (Roberts & Fishman, 2021; Mota et al., 2025).

Taken together, the practical response to altered host immunity is not a new diagnostic test, but a different method of interpretation. The clinician should first define the immune context, then decide whether the presentation is under-expressed, misdirected, or concordant, and finally judge the case by the consistency of the overall pattern instead of by an isolated sign. Earlier imaging, reassessment, and escalation become appropriate when the clinical picture appears either deceptively mild or non-specifically noisy.

Conclusion

Endodontic diagnosis depends on the relationship between microbial irritation and host response. Altered host immunity weakens that relationship and makes conventional findings less straightforward to interpret. The central message of this review is therefore not that conventional diagnostic methods lose value, but that their findings require more careful interpretation when host immunity is altered.

This review has argued for a practical distinction between immune suppression, immune dysregulation, and overlap states. That distinction helps explain why diagnostic error may occur in different directions, from under-recognition of biologically important infection to over-interpretation of non-specific oral symptoms. Under these conditions, safer diagnosis depends on integration of medical history, tooth-specific examination, imaging, and reassessment over time. The clinician should resist the temptation to rely on one reassuring sign or one apparently obvious symptom when the wider pattern is discordant.

There is also a human side to this diagnostic problem. Patients with altered host immunity often arrive with complex medical histories, repeated treatment experiences, and symptoms that do not fit the usual endodontic pattern. Some have been through chemotherapy, transplantation, autoimmune disease flares, or long periods of oral discomfort that are difficult to explain. Others may feel anxious because symptoms are real, but the source is uncertain. In these situations, patience is not simply a personal virtue. It is part of good clinical judgement. A careful pace, close listening, and willingness to review a case more than once may prevent both under-treatment and unnecessary intervention.

Empathy is equally important. When findings are equivocal, patients still need to feel that their symptoms are recognized and taken seriously. A calm explanation of uncertainty, an honest account of what is known and what is still unclear, and a stepwise plan for review or escalation can reduce fear and build trust. In patients whose disease expression is altered by immune dysfunction or immune modifying treatment, that trust has practical value because it allows diagnosis to proceed with greater clarity and less distress.

Ultimately, altered host immunity does not call for a different specialty of diagnosis. It calls for a more thoughtful one. The clinician must be more alert to under-expressed disease, more cautious with non-specific symptoms, and more prepared to combine evidence derived from history, examination, imaging, and medical context. Good care in these patients depends not only on diagnostic skill, but also on patience, humility, and empathy.

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