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When silence turns to pain: Decoding endodontic flare-ups

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ABSTRACT

Endodontic flare-up remains one of the most clinically challenging and unpredictable complications of root canal therapy, turning a relatively routine procedure into an acute emergency with sudden onset of pain and/or swelling within hours to days of an appointment. Although it has been studied for decades, the multifactorial etiology with microbial, mechanical, chemical and immunological factors still challenge clinicians in terms of its predictable prevention and management. This review aims to collate current evidence on the definition, epidemiology, classification, etiopathogenesis and risk factors of endodontic flare-ups, with particular emphasis on the roles of microbial persistence (especially *Enterococcus faecalis*), host inflammatory mediators and iatrogenic factors such as apical extrusion of debris and irrigants. Evidence-based preventive and management strategies ranging from occlusal reduction, intracanal medicaments, pharmacological control of pain and inflammation to judicious use of antibiotics are discussed along with contemporary diagnostic aids such as cone beam computed tomography and emerging artificial intelligence assisted radiographic analysis. We propose a clinical decision-making algorithm to assist the practitioner from diagnosis to resolution. The overall incidence of severe flare-up is low (2-9% in contemporary series), but its unpredictable nature and impact on patient trust mean that there is a need for continued research into individualized risk stratification and minimally invasive prevention.

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INTRODUCTION

For the vast majority of patients' root canal treatment is a routine procedure to relieve pain rather than cause it. However, a small but clinically relevant percentage of patients experience an unanticipated exacerbation of pain, swelling or both between or after endodontic appointments; an event that is universally recognized in the specialty as a "flare-up" (Alves, 2010; AAE, 2017). The phrase "when silence turns to pain" captures the essential unpredictability of this phenomenon: a tooth that was quiescent, or a treatment that proceeded uneventfully at the chair, can within hours evolve into a genuine dental emergency requiring an unscheduled visit (Ohshima *et al.*, 2026; Alves, 2010). Flare-ups are much more important than the immediate discomfort they cause.

They erode patient trust in the clinician and in endodontic therapy more generally, they consume unplanned chair time, they may generate medicolegal concern where communication has been inadequate, and in rare instances they may presage a spreading odontogenic infection with systemic consequences (AAE, 2017). In particular, an unexpected flare-up can be professionally unsettling for the postgraduate trainee and the early-career clinician, leading to unnecessary self-doubt about technique, when in the majority of cases the event reflects the underlying biology of the case rather than a procedural error (Ohshima *et al.*, 2026; Onay *et al.*, 2015). Knowing why flare-ups happen, who is at highest risk and how they can be prevented and managed is therefore central to safe, evidence-based endodontic practice and to the maintenance of the clinician-patient relationship upon which long-term treatment success ultimately depends.

This review reviews the definition, history, epidemiology, classification, pathophysiology, risk factors, microbiology, diagnosis, prevention, and management of endodontic flare-ups, and summarizes the role of modern imaging and artificial-intelligence-supported tools in this changing landscape, concluding with a practical clinical decision-making algorithm for chairside use.

WHAT IS AN ENDODONTIC FLARE-UP?

An endodontic flare-up is most commonly defined as the occurrence of severe pain and/or swelling following root canal treatment requiring an unscheduled emergency visit as opposed to the mild-to-moderate, self-limiting discomfort which is a common and expected sequela of instrumentation (Alves, 2010). Similarly, the glossary of the American Association of Endodontists defines flare-up as an acute exacerbation of peri radicular pathosis following the initiation or continuation of root canal treatment. The key diagnostic threshold is not simply the presence of pain, which is almost universal in the first 24–48 hours after treatment, but its severity, its association with objective swelling and most operationally, whether it drives the patient to seek unplanned care (Alves, 2010).

VIEWPOINT OF HISTORY

The clinical interest in unpredictable post-treatment flare-ups dates back to the earliest era of modern endodontics, when practitioners such as Seltzer and Morse documented "flare-ups" during the course of multi-visit treatment of necrotic, peri apically involved teeth. Instrumentation and the use of antibiotics were also pointed out by early researchers as possible etiologies, along with psychosomatic and stress-related factors. This is reflective of the still evolving understanding of pulpal and periapical immunology at the time. In subsequent decades the emphasis increasingly focused on microbiologic persistence, especially resistant facultative anaerobes that survive canal disinfection, and iatrogenic mechanical and chemical injury from instrumentation and irrigation. Nickel-titanium rotary instrumentation, standardized irrigation protocols, cone-beam computed tomography and, more recently, artificial-intelligence-assisted diagnostics have all slowly improved not only the understanding but also the prevention of flare-up, although complete elimination remains elusive.

EPIDEMIOLOGY AND INCIDENCE

The reported incidence of flare up in the literature varies widely, reflecting the differences in definition, study design, population and operator experience. A

large systematic review and meta-analysis pooling fifteen eligible studies and 24,320 treated cases reported a total incidence of severe flare-up of 2.83% (Ohshima *et al.*, 2026). Reported retrospective cohorts have ranged from 2% (1,725-patient series) (Nair *et al.*, 2017) to 3.2% (1,819-tooth cohort) (Onay *et al.*, 2015), 8.5% (prospective multi-visit series) (Gbadebo *et al.*, 2016), and 9.4% (1,000-patient retrospective cohort) (Magar *et al.*, 2022). In general, recent estimates suggest that the incidence of clinically significant flare-up in normal circumstances varies between about 2-9%, but rates up to 50% have been reported in high-risk situations such as retreatment of teeth with existing periapical lesions (Alves, 2010). This wide range emphasizes that flare-up risk is not an inherent feature of root canal treatment per se but is heavily modulated by case selection, pulpal and periapical status and operator technique.

CLASSIFICATION OF ENDODONTIC FLARE UPS

Flare-ups are traditionally categorized along several overlapping axes (Alves, 2010). They may be classified by dominant symptom as painful (minimal or no swelling), swelling-predominant, or mixed pain and swelling. Interappointment flare-up is seen between visits in multi-visit treatment by timing, whereas post obturation flare-up occurs after completion of treatment. Mild cases are managed with reassurance and analgesics, moderate cases may need an unscheduled visit for occlusal adjustment or change of medicament, severe cases have marked swelling, spreading infection or systemic signs requiring incision and drainage and/or systemic antibiotics (AAE, 2017). Another useful distinction is between flare-ups arising in vital, previously untreated teeth and those arising in necrotic, previously infected or retreatment cases, as etiology and management differ meaningfully between these groups (Ohshima *et al.*, 2026; Nair *et al.*, 2017).

ETIOPATHOGENESIS

The cause of endodontic flare-up is truly multifactorial involving microbial, mechanical, chemical and immunological factors working together rather than independently (Ohshima *et al.*, 2026; Alves, 2010).

Microbial factors

The most frequent reason for flare-up is thought to be the persistence or re-introduction of microorganisms in the root canal system or their forced extrusion into the periapical tissues during instrumentation. Facultative anaerobes that can withstand the harsh, nutrient-limited, high-pH environment created by canal disinfection, particularly Enterococcus faecalis, are consistently over-represented in secondary and persistent endodontic infections, with rates of detection reported as high as 77-89.6% in retreatment cases compared with substantially lower rates in primary infections (Ardila *et al.*, 2026; Elashiry *et al.*, 2023). Such persistence is accomplished by *E. faecalis* through dentinal tubule invasion, resistance to alkaline pH and nutrient deprivation, and formation of resilient biofilms that protect the organism from host defenses and antimicrobial irrigants and medicaments (Elashiry *et al.*, 2023; Yang *et al.*, 2024). *E. faecalis* and other organisms including black-pigmented anaerobes of the genus *Porphyromonas*, notably *P. gingivalis* and *P. endodontalis* have been historically associated with the acute symptomatology characteristic of interappointment flare-up. This reflects the broader principle that a shift in canal microbial ecology to more virulent or resistant organisms, rather than the mere presence of bacteria per se, underlies acute exacerbation. Bacterial lipopolysaccharide and other antigenic by-products released into the periapex are potent stimuli for the host inflammatory cascade described below. This ecological complexity, rather than a single causative organism, is likely to be the reason why antimicrobial measures alone, despite substantial advances in irrigation and instrumentation technology, have failed to completely eliminate the risk of flare-ups.

Kinematic factors

Mechanical injury to the periodontal ligament and periapex is a result of over instrumentation beyond

the apical constriction, aggressive canal enlargement and extrusion of infected dentine debris into periapical tissues, irrespective of any microbial contribution (Tanalp, 2022). Even in cases with minimal preoperative microbial load such trauma can elicit a self-limited inflammatory flare. The degree of debris and irrigant extrusion has been shown to vary with root canal curvature, instrumentation kinematics and irrigant delivery technique (Tanalp, 2022). Missed canals, ledging and incomplete debridement of the canal system leave residual irritants in situ and predispose to delayed exacerbation.

Chemical factors

Irrigants, such as sodium hypochlorite, and medicaments, such as calcium hydroxide, are strong tissue irritants in the event that they are accidentally extruded beyond the apex (Tanalp, 2022). Hypochlorite accidents are not common, but result in a dramatic and immediate inflammatory response due to direct chemical injury to periapical soft tissue. Even subclinical apical extrusion of irrigant or medicament during routine treatment may contribute to lower grade postoperative inflammation and pain in susceptible individuals (Tanalp, 2022).

Immune response

Whatever the insult leading to it, the final common pathway of flare up is the activation of the host innate and adaptive immune response within the periapical tissues, leading to the release of pro-inflammatory mediators and neuropeptides such as substance P and calcitonin gene-related peptide that sensitize nociceptors and increase local vascular permeability (Caviedes *et al.*, 2018), as explained in the following section.

PATHOLOGY

Mechanical or chemical means disrupt microbial antigens and tissue debris release, activating resident and recruited immune cells in the periapical tissues. This leads to the arachidonic acid cascade with production of prostaglandins (notably PGE2) and leukotrienes, and release of pro-inflammatory cytokines, including interleukin-1beta, interleukin-6 and tumor necrosis factor-alpha. At the same time, neuropeptides such as substance P and calcitonin gene-related peptide mediate neurogenic inflammation, which worsens vasodilation and plasma extravasation, with the instrumentation itself found to upregulate the expression of these neuropeptides in the periodontal ligament (Caviedes *et al.*, 2018). The net effect is an increase in vascular permeability, edema formation within the rigid non-compliant confines of the periapical and periodontal ligament space and a consequent rise in local tissue pressure. Because of limited capacity of the periapical tissues to accommodate this edema, even small increases in tissue fluid because exaggerated pressure increase that directly stimulates and sensitizes peripheral nociceptors, resulting in spontaneous pain, percussion tenderness, and in severe cases, clinically obvious swelling (Fig. 1) (Ohshima *et al.*, 2026; Caviedes *et al.*, 2018). This mechanistic cascade accounts for the usual delay (hours, as mediator synthesis and diffusion occur) between the initiating event and the onset of symptoms, and for the self-limited nature of most episodes once the causative irritant has been removed and the inflammatory response has subsided.

RISK FACTORS

A significant amount of clinical evidence has investigated patient-related, tooth-related and operator-related variables associated with the risk of flare-up (Fig. 2). The strongest modern evidence is from a systematic review and meta-analysis of fifteen studies and over 24,000 cases published in 2026. The significant risk factors reported were female sex, mandibular tooth, non-vital pulp, preoperative spontaneous pain, presence of a periapical lesion, multiple-visit treatment, retreatment and preoperative percussion pain, with preoperative spontaneous pain (relative risk 5.83) and percussion pain (relative risk 3.45) having the strongest association (Ohshima *et al.*, 2026). Interestingly, this analysis did not show a significant association with patient age, tooth type, number of root canals, instrumentation technique, or preoperative analgesic

use (Ohshima *et al.*, 2026). A Monte Carlo simulation to rank the relative importance of candidate risk factors also found periapical lesion, multiple-visit treatment and preoperative pain to be among the most influential, with retreatment, female gender, necrotic pulp status and analgesic use ranking comparatively lower in sensitivity (Akshoy *et al.*, 2021). Independent retrospective cohorts support the importance of preoperative pain and pulpal/periapical diagnosis. In one series, asymptomatic irreversible pulpitis was identified as carrying the highest flare-up risk (10%), followed by necrotic pulp with (2.7%) and without (2.1%) an associated periapical lesion (Nair *et al.*, 2017). Another study found that preoperative pain was the dominant risk factor, accounting for the majority of flare-up episodes occurring at the critical first visit of multi-visit treatment (Gbadebo *et al.*, 2016).

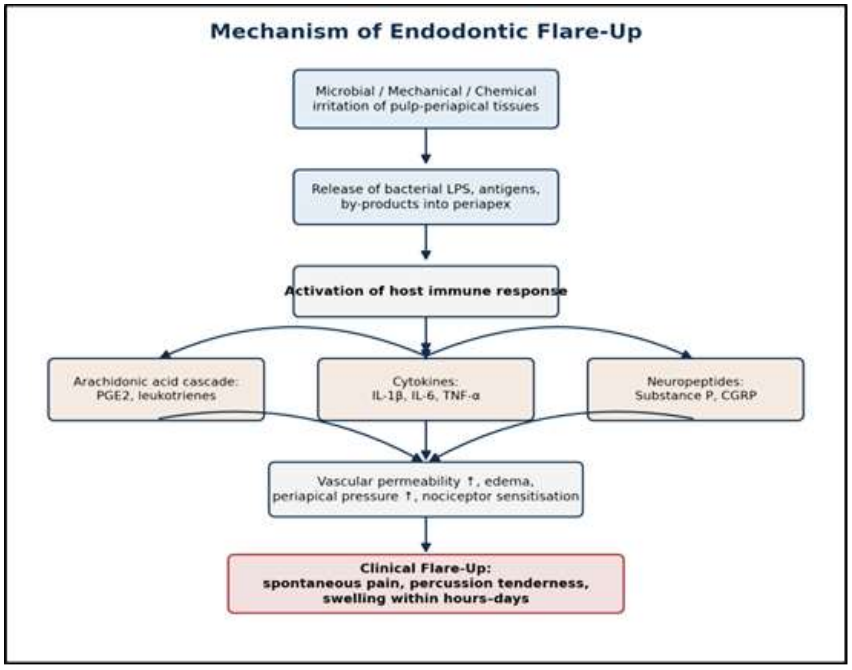


Fig. 1. Endodontic flare-up mechanism: from irritant to clinical exacerbation

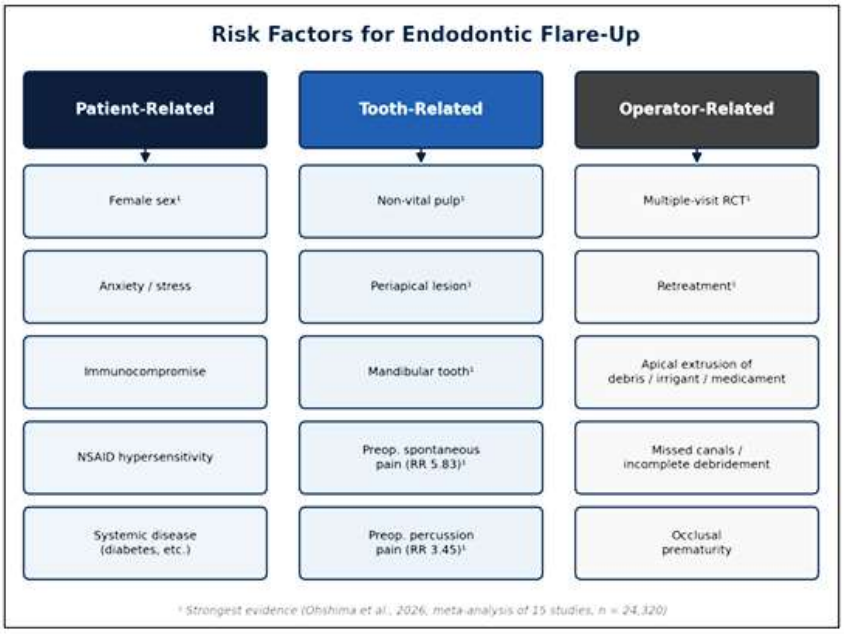


Fig. 2. Summary of patient, tooth and operator related risk factors for endodontic flare ups

In contrast, some cohorts have not found a significant effect of age, gender, tooth type, number of canals, choice of irrigant or status of retreatment (Onay *et al.*, 2015), indicating that risk-factor profiles are not perfectly consistent across populations and settings and that the single most reproducible predictor across studies is preoperative symptomatology.

ENDODONTIC FLARE-UPS: MICROBIOLOGY

Enterococcus faecalis is the main microbial pathogen involved in the microbiology of persistent and secondary endodontic infection and consequently, to flare-up pathogenesis. This Gram-positive facultative anaerobe is recognized for its extraordinary environmental resilience, withstanding extreme alkaline pH and nutrient deprivation lethal to most competing organisms, invading dentinal tubules to depths impervious to standard instrumentation and irrigation, and expressing virulence factors such as aggregation substance that promote adhesion, immune evasion and resistance to macrophage killing (Ardila *et al.*, 2026). Its ability to form structurally resilient biofilms further insulates it from both host immune defenses and antimicrobial agents and is thought to be a major factor in its disproportionate presence in post-treatment apical periodontitis, with detection rates of 45.8% or more in previously treated, persistently infected canals (Yang *et al.*, 2024). Many strategies have been studied recently to overcome E. faecalis biofilm resistance, including the use of antisense RNA against two-component signal transduction systems, bacteriophage therapy, nanoparticle-mediated antimicrobial photodynamic therapy and enzymatic biofilm disruption using cellulase adjuvants (Elashiry *et al.*, 2023), indicating the difficulty in achieving durable canal disinfection with this organism and, ultimately, in preventing flare-up in retreatment cases.

CLINICAL FEATURES AND DIAGNOSIS

Clinically, a flare-up will usually present itself as a spontaneous, throbbing pain, disproportionate tenderness to percussion and biting and, in more advanced cases, localized or diffuse swelling of soft tissue, which may or may not be fluctuant, within hours to a few days of an endodontic appointment (Alves, 2010). Systemic features like low-grade fever, malaise or regional lymphadenopathy suggest a more advanced inflammatory or frankly infective process and deserve closer attention (AAE, 2017). Diagnosis is based on a combination of a targeted history confirming the timing of recent treatment, clinical examination with percussion, palpation, assessment of mobility, and examination for sinus tract or fluctuance, and periapical radiography to exclude procedural complications such as missed canals, perforation, instrument separation, or gross overextension of obturation material.

DIFFERENTIAL DIAGNOSES

Not all post-treatment pain is a true flare-up and careful differential diagnosis is essential before instituting management (Alves, 2010). Other possibilities include normal and self-limiting postoperative discomfort caused by instrumentation trauma, occlusal prematurity on a restoration or temporary filling, a missed canal or untreated pulpal remnant, vertical root fracture, characterized by a narrow and deep periodontal probing defect and a J-shaped radiolucency, periodontal abscess of non-endodontic origin, sinusitis mimicking referred maxillary posterior tooth pain, and less commonly temporomandibular disorder or atypical facial pain syndromes mimicking odontogenic pain, but not responding to endodontic intervention. By systematically excluding these mimics, unnecessary retreatment or overtreatment of a tooth with a non-endodontic source of pain is prevented.

RADIOGRAPHIC AND ADVANCED DIAGNOSTIC AIDS

Conventional intraoral periapical radiography remains the imaging modality of choice, but its two-dimensional nature limits sensitivity for early or anatomically complex periapical pathology. Cone-beam computed tomography (CBCT) gives a three-dimensional view of the periapical bone architecture, leading to earlier and more precise detection of periapical lesions, better definition of root canal

anatomy including missed canals, and more accurate identification of procedural complications such as perforation or extruded material, which can be relevant when investigating a flare-up. Artificial intelligence aided image analysis has rapidly evolved as an adjunct to both 2D and CBCT interpretation. Deep-learning models, especially convolutional neural network architectures, have shown diagnostic accuracy in periapical lesion detection ranging from 75% to 99% with sensitivity and specificity often above 80-90% in intraoral, panoramic, and CBCT modalities (Aloufi, 2026; Doumani *et al.*, 2005), and scoping reviews of CBCT-based AI applications indicate that such systems can decrease diagnostic time, enhance consistency, and assist less experienced clinicians in lesion detection, classification, and segmentation (Karobari *et al.*,2026). There is a growing scope of AI applications in endodontics beyond lesion detection, ranging from prediction of treatment outcome from preoperative radiographs, working-length determination, and identification of root fractures and canal morphology variations (Setzer *et al.*, 2024), and these tools are becoming an increasingly relevant adjunct to conventional diagnostic pathways in complex or refractory cases, including those complicated by flare-up.

PREVENTING ENDODONTIC FLARE-UPS

Prevention is used in the pre-operative, intra-operative and post-operative phases of treatment (Fig. 3) (Alves, 2010).

Preoperative interventions

Accurate pulpal and periapical diagnosis based on pulp sensibility testing and radiographic assessment is possible, and realistic risk stratification is possible, since teeth with spontaneous preoperative pain or percussion tenderness carry a substantially elevated flare up risk (Ohshima *et al.*, 2026). It is important to communicate clearly with the patient the potential for post-operative discomfort, especially in the presence of high-risk factors, so that expectations are managed and the chance that an expected mild discomfort is misinterpreted as a true emergency is minimized.

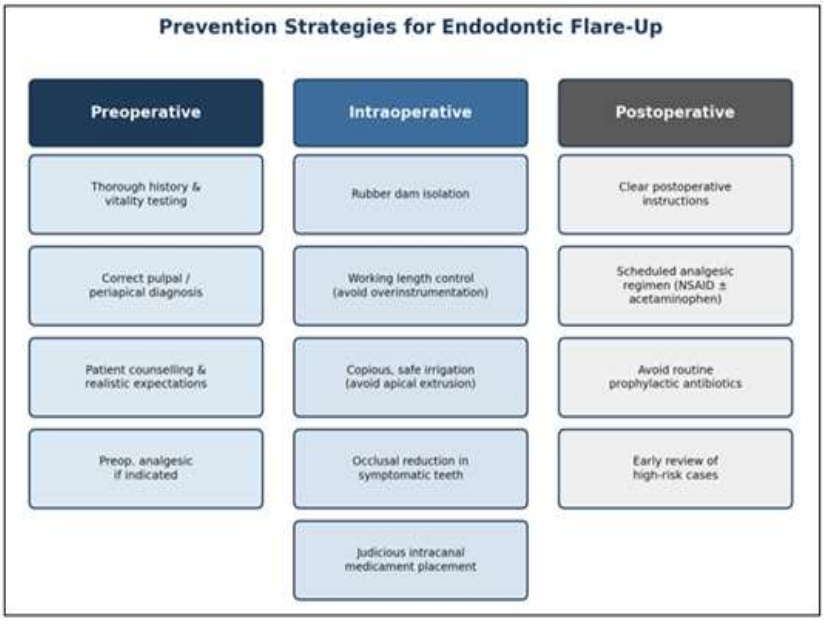


Fig. 3. Preventive strategies: preoperative, intraoperative, and postoperative

Intraoperative measurements

Rubber dam isolation, conservative and well-controlled working length determination to avoid over instrumentation, copious but controlled irrigation designed to minimize apical extrusion (Tanalp, 2022), and thorough but atraumatic debridement, all serve to reduce microbial load and mechanical/chemical injury to periapical tissues. There is a substantial evidence base for occlusal reduction in teeth with pre-treatment percussion

sensitivity. One randomized controlled trial in mandibular posterior teeth with symptomatic irreversible pulpitis and percussion sensitivity found occlusal reduction decreased the risk of moderate-severe pain by approximately 40% at 12 hours and reduced overall pain risk by 25% at 24 hours post-instrumentation (Ahmed *et al.*, 2020). One systematic review and meta-analysis of randomized trials found occlusal reduction decreased postoperative pain at six days for teeth with irreversible pulpitis (Nguyen *et al.*, 2020). However, this evidence is not fully consistent, as another systematic review and meta-analysis registered with PROSPERO found occlusal reduction did not significantly impact pain within the first 48 hours (Chagas *et al.*, 2021), and a comparative trial found benefit limited to the early 12-hour interval after both instrumentation and obturation (Emara *et al.*, 2019). This illustrates that occlusal reduction, while low risk and generally preferred as an adjunct, should not be considered a consistently decisive preventive measure.

Post-operative care

The main preventive measures postoperatively are judicious use of intracanal medicaments between visits (Eftekhar *et al.*, 2013; Negm, 2001; Wagh *et al.*, 2022), scheduled (rather than as needed) analgesic dosing for the first 24 to 48 hours in higher risk cases, and avoidance of routine prophylactic systemic antibiotics, which are not supported by current evidence in the absence of signs of spreading infection (Milani *et al.*, 2022; Cope *et al.*, 2024). Early telephone or face-to-face review of preoperatively identified high-risk patients allows early intervention should symptoms develop.

MANAGEMENT OF ENDODONTIC FLARE-UPS

Once a flare-up has developed, the management of the flare-up follows a logical, stepwise sequence (Fig. 4) (AAE, 2017).

Reinstatement of drain

The single most important step in the resolution of an established flare-up is to establish drainage, either through the canal system itself, incision and drainage of a fluctuant soft-tissue swelling or, rarely, trephination through bone in cases of localized periapical abscess without an intraoral pathway. This directly relieves the elevated periapical tissue pressure responsible for pain (AAE, 2017).

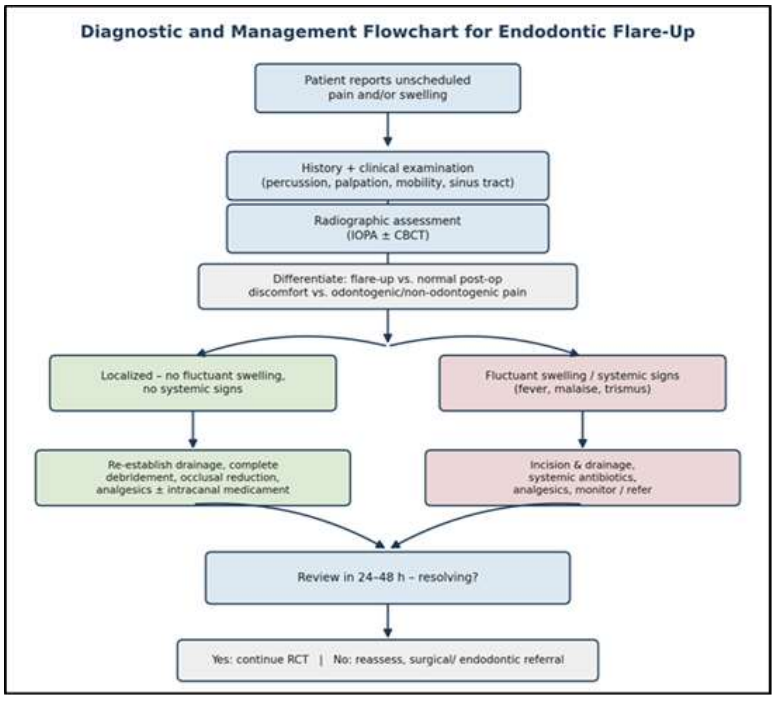


Fig. 4. Suspected endodontic flare-up–diagnostic and management flowchart

Reduction of occlusion

Occlusal reduction of teeth tender to percussion will remove a mechanical trigger for pain during function and is a simple low-morbidity adjunct, supported by several, although not universally consistent, randomized trials (Ahmed *et al.*, 2020; Nguyen *et al.*, 2020; Emara *et al.*, 2019).

Intracanal medicaments

Calcium hydroxide continues to be the gold standard interappointment medicament due to its antimicrobial and tissue-modulating properties. Corticosteroid-containing preparations, alone or combined with an antibiotic (as in classic corticosteroid-antibiotic compounds), have shown a significant reduction in spontaneous pain and percussion sensitivity compared with placebo or control medicaments in several randomized trials (Eftekhar *et al.*, 2013; Negm, 2001). This is in keeping with their ability to inhibit the inflammatory mediator cascade discussed in the pathophysiology section. A systematic review of the incidence of flare-up after intracanal medicament placement concluded that medicaments do not themselves precipitate flare-up and, if anything, decrease interappointment pain when used appropriately (Wagh *et al.*, 2022). In randomized trials (Omaia *et al.*, 2025), the adjunctive use of anti-inflammatory agents in combination with antimicrobial pastes has also been shown to be beneficial in reducing postoperative pain in necrotic, asymptomatic teeth.

Irrigation instructions

Adequate irrigation with sodium hypochlorite at the right concentration, delivered with a side-vented needle placed short of the binding point to minimize apical extrusion, is still the cornerstone in the management of an active flare-up (Tanalp, 2022). A final rinse with EDTA to remove the smear layer that improves subsequent medicament and sealer contact with dentine. Care must be taken to avoid pressure driven extrusion of irrigant beyond the apex, itself a potential contributor to chemical flare-up (Tanalp, 2022).

Pharmacologic treatment

The first-line analgesic management includes non-steroidal anti-inflammatory drugs, alone or in combination with acetaminophen, which directly target the prostaglandin-mediated inflammatory cascade and are usually more effective than opioid analgesics in the inflammatory pain of flare-up, while avoiding the sedation, dependence risk, and gastrointestinal or central side effects associated with opioid use. In situations where NSAIDs are contraindicated (e.g., patients with peptic ulcer disease, significant renal impairment or aspirin-exacerbated respiratory disease), acetaminophen alone or corticosteroid-based alternatives may be considered. Multiple randomized trials and a Cochrane systematic review have demonstrated no significant benefit of systemic antibiotics over placebo in terms of pain, swelling or flare-up incidence in localized, immunocompetent cases managed with adequate debridement and drainage (Morse *et al.*, 1987; Milani *et al.*, 2022; Cope *et al.*, 2024). Systemic antibiotics are only indicated where there is evidence of a spreading infection, systemic involvement or in medically compromised patients. Professional guidance has been informed by the evidence base to discourage routine prescription of antibiotics for uncomplicated apical periodontitis or abscess (AAE, 2017), despite documented widespread over-prescription in contemporary practice surveys (Mendez *et al.*, 2022). This pattern is directly relevant to global antimicrobial stewardship efforts and one that dental education programs are increasingly seeking to address. Historical prophylactic antibiotic trials in asymptomatic, necrotic teeth did show lower incidence of flare-ups with peri treatment antibiotic coverage (Morse *et al.*, 1987), however this must be balanced with the risks of hypersensitivity, resistance selection, and adverse effects, and is not representative of current evidence-based recommendations for routine use. When indicated, penicillin-based regimens are still first-line in non-allergic patients, with clindamycin or metronidazole limited to penicillin-allergic individuals or in case of an anaerobic-predominant clinical picture.

Surgical therapy

In the few cases where conservative measures do not resolve the lesion, where the anatomy is complex and does not allow adequate canal drainage, or where a persistent sinus tract or localized abscess does not respond to conservative measures, surgical intervention may be required including incision and drainage, apicoectomy, or in cases with a poor prognosis, extraction (AAE, 2017).

Role of modern technology

Several technologies are revolutionizing the diagnostic and management scenario for endodontic flare-up and the periapical disease that predispose to it (Aloufi, 2026; Setzer *et al.*, 2024).

3D CBCT

In addition, as described in Section 12, CBCT improves the detection of periapical pathology and procedural complications that might be overlooked by traditional radiography, permitting a more accurate diagnosis when a flare-up occurs in the presence of equivocal two-dimensional findings (Karobari *et al.*, 2026).

Navigation moving

Dynamic navigation systems have been adapted from implant surgery and are increasingly being explored as a method for guided access cavity preparation and canal location in calcified or anatomically challenging teeth. Systematic review evidence suggests that such systems improve precision, accuracy and efficiency in locating canals over the freehand technique with greater preservation of dentine (Vasudevan *et al.*, 2022), with the potential to reduce iatrogenic mechanical injury and missed canals that predispose to later flare-up, though evidence specific to flare-up reduction itself remains limited.

Laser-assisted endodontics

The use of laser-activated irrigation has been proposed as an alternative to conventional syringe irrigation for enhanced removal of debris and smear layer as well as increased disinfection of complex canal anatomy, which could result in a decreased residual load of microbial and organic irritants. A systematic review provided evidence that laser-activated irrigation may be associated with a small reduction in postoperative pain in the first 24-48 hours compared to conventional needle irrigation; however, the certainty of this evidence is low and the effect does not persist to day three or seven (McGillvray *et al.*, 2024).

Photodynamic therapy (PDT)

Antimicrobial photodynamic therapy, in which a photosensitizer activated by light of a specific wavelength generates reactive oxygen species, has been shown to effectively reduce Enterococcus faecalis biofilm viability in laboratory studies, including the use of nanoparticle-enhanced formulations to improve the targeting and penetration of the photosensitizer (Elashiry *et al.*,2023). This represents a promising adjunct to conventional chemo mechanical disinfection in persistent or retreatment cases at high risk of flare-up.

Artificial intelligence

In addition to diagnostic imaging, AI-based tools are being investigated for prediction of treatment outcome (Setzer *et al.*, 2024), and more speculatively, for risk stratification of patients for flare-up using integrated clinical, radiographic, and historical data, an application that is still in the early stages of investigation (Doumani *et al.*, 2005).

CLINICAL RECOMMENDATIONS AND EVIDENCE BASED GUIDELINES

On the basis of the evidence reviewed above, several practical recommendations emerge. Preoperative symptoms, such as spontaneous pain and percussion tenderness, are the most reproducible predictors of the risk of flare-up and should be used to guide case-specific counseling and postoperative planning (Ohshima *et al.*, 2026). Second, occlusal reduction is a low-risk evidence-based adjunct for symptomatic teeth with percussion tenderness, although the magnitude and duration of benefit varies across trials (Ahmed *et al.*, 2020; Nguyen *et al.*, 2020; Chagas *et al.*, 2021; Emara *et al.*, 2019).

Thirdly, there is a reasonable evidence base for intracanal medicaments with corticosteroids to reduce inter-appointment pain in symptomatic cases (Eftekhar *et al.*, 2013; Negm, 2001). Fourthly, and most importantly, systemic antibiotics should not be routinely prescribed for prevention or treatment of uncomplicated flare-up in immunocompetent patients with localized disease but should be reserved for cases with clear evidence of spreading infection or systemic compromise, in accordance with Cochrane-level evidence and professional society guidance (Milani *et al.*, 2022; Cope *et al.*, 2024; AAE, 2017).

RECENT PROGRESS AND NEW TREATMENTS

New approaches to target the microbiological basis of persistent infection and flare-up include antisense RNA technology against E. faecalis two-component signal transduction systems to inhibit virulence gene expression and biofilm formation, bacteriophage therapy against clinical E. faecalis isolates including antibiotic resistant strains, nanoparticle-enhanced antimicrobial photodynamic therapy for deeper and more effective biofilm disruption, and enzymatic adjuvants such as cellulase to potentiate conventional antibiotic activity against biofilm-embedded organisms (Elashiry *et al.*, 2023). At the same time, diagnostic tools using deep learning are rapidly maturing, with recent systematic reviews reporting periapical lesion detection diagnostic accuracies that are comparable to or better than those of experienced clinicians in several comparative studies (Aloufi, 2026; Doumani *et al.*, 2025), suggesting a near-term role for AI-assisted triage and monitoring of at-risk cases.

PATHWAY OF CLINICAL DECISION-MAKING

Fig. 4 shows an integrated diagnostic/management flowchart, and Fig. 5 is a focused clinical management algorithm for an established flare-up. To summarize, the clinician first confirms the diagnosis of flare-up against the differential diagnoses in Section 11, then proceeds with drainage, completion of debridement, and occlusal adjustment as needed, followed by selection of an appropriate intracanal medicament and analgesic regimen, with systemic antibiotics and/or surgical referral reserved for cases with systemic involvement or spreading infection.

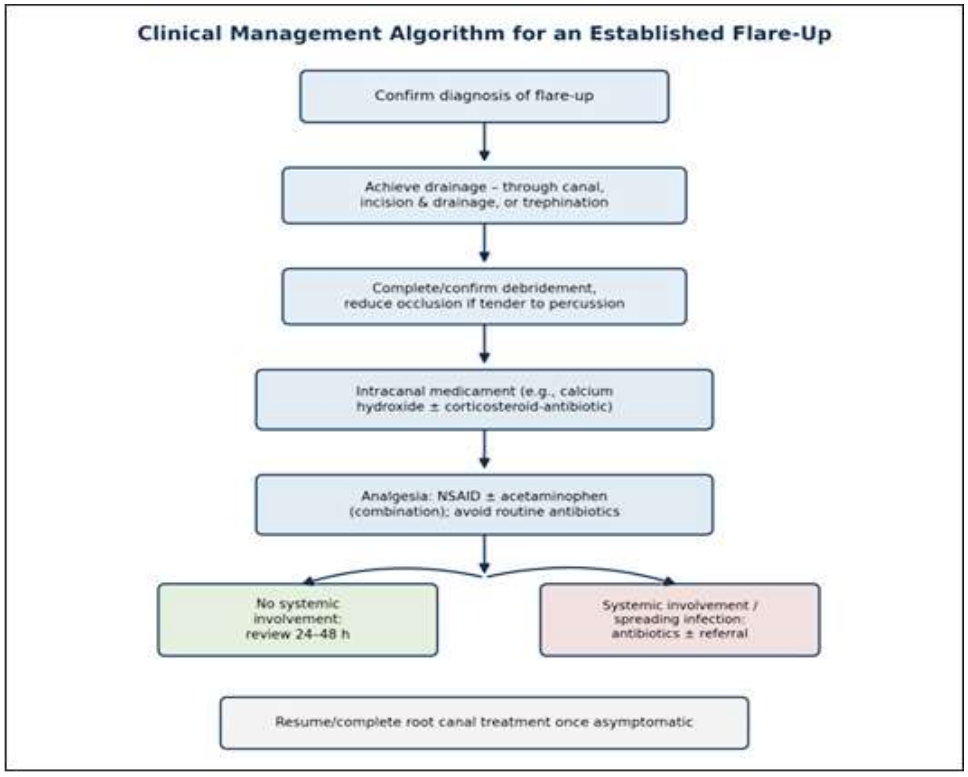


Fig. 5. Algorithm for the clinical management of an established endodontic flare-up

MODERN DEBATES AND CONTROVERSIES

There are several aspects of real uncertainty that remain in the flare-up literature. The efficacy of occlusal reduction is controversial. Some randomized trials and meta-analyses report significant benefit (Ahmed *et al.*, 2020, Nguyen *et al.*, 2020) while others report no significant effect in the critical first 48 hours (Chagas *et al.*, 2021), probably reflecting heterogeneity in case selection, reduction technique and outcome timing across studies. The effect of single- versus multiple-visit treatment on risk of flare-up is also controversial. Multiple-visit treatment has been identified as a risk factor in several analyses (Ohshima *et al.*, 2026; Aksoy *et al.*, 2021) but this association may be partly confounded by indication, with more complex or symptomatic cases preferentially treated over multiple visits. Likewise, the value of routine intracanal medicament placement versus single-visit obturation is a matter of conflicting opinion, weighed against the proven advantage of corticosteroid medicaments in symptomatic cases versus the theoretical benefits of reducing bacterial re-entry with single-visit treatment. Finally, in real-world practice, prescribing patterns still show significant over-prescription (Mendez *et al.*, 2022), although high-level evidence against routine antibiotic use has remained high, showing an ongoing gap between evidence and practice that has not yet been fully closed by education and dissemination of guidelines.

FUTURE PROSPECTS

Future research directions include the development of validated individualized risk prediction models combining clinical, radiographic and possibly microbiological or biomarker data to identify patients at truly increased risk of flare-up before the start of treatment (Ohshima *et al.*, 2026; Doumani *et al.*, 2025). Further clarification of the comparative efficacy of specific intracanal medicaments and occlusal management protocols, using adequately powered, standardized randomized trials (Chagas *et al.*, 2021; Wagh *et al.*, 2022). Further refinement of AI-assisted diagnostic and risk stratification tools, with prospective validation in real-world clinical settings (Aloufi, 2026; Setzer *et al.*, 2024; Karobari *et al.*, 2026). Further exploration of targeted antimicrobial strategies against Enterococcus faecalis biofilms that might reduce the persistent-infection burden underlying retreatment-associated flare-up risk (Elashiry *et al.*, 2023).

CLINICAL RELEVANCE

For the practicing clinician, the recognition that preoperative pain and percussion sensitivity are the most powerful predictors of flare-up (Ohshima *et al.*, 2026) allows targeted counselling, closer post-operative monitoring and pre-emptive use of low risk adjuncts such as occlusal reduction in appropriately selected cases [8,10]. The discipline of not using antibiotics when there is no systemic or spreading infection is equally important, both to ensure that practice is consistent with the evidence base (Milani *et al.*, 2022; Cope *et al.*, 2024) and to support broader antimicrobial stewardship goals (Mendez *et al.*, 2022; AAE, 2017). The most reliable way to rapidly resolve symptoms is a structured, stepwise approach to management with drainage and mechanical/chemical debridement as the front line rather than escalation of pharmacology.

LIMITATIONS OF THE CURRENT EVIDENCE

There is a lot of variation in the flare-up literature in how cases are defined – some studies require an unscheduled emergency visit and others only use patient-reported pain scores – making it difficult to directly compare across studies. However, even the largest meta-analysis of the current literature (Ohshima *et al.*, 2026) has a low certainty of evidence for many of the reported risk factors when assessed with GRADE. This reflects the mainly observational nature of the underlying studies and the difficulty in controlling for confounding variables such as case complexity and operator experience. Randomized trial evidence for specific interventions, especially occlusal reduction, remains inconsistent in both direction and magnitude of effect (Ahmed *et al.*, 2020; Vianna *et al.*, 2020; Chagas *et al.*, 2021; Almasoud *et al.*, 2025). Long term, multi-centre, adequately powered trials remain relatively few compared with the clinical importance of the problem.

CONCLUSION

Endodontic flare-up is a multifactorial, incompletely predictable complication of root canal treatment, arising from the interaction of microbial persistence, mechanical and chemical injury and host inflammatory response within the confined anatomical space of the periapical tissues. Although the overall incidence is modest in current practice, specific clinical presentations, particularly teeth with spontaneous preoperative pain and percussion tenderness, are at a substantially higher risk and merit focused preventive strategies. A structured approach including accurate preoperative diagnosis, meticulous intraoperative technique, judicious use of occlusal reduction and intracanal medicaments, evidence-based (not reflexive) use of systemic antibiotics and a clear stepwise management algorithm provides the best available pathway for clinicians to minimize both the incidence and impact of this challenging complication. Continued research into individualized risk prediction, targeted antimicrobial strategies against resistant organisms such as *Enterococcus faecalis*, and AI-assisted diagnostic support promises further refinement of this pathway in the years ahead.

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