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Persistent apical periodontitis: Current Understanding and Recent Advances in Management

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Abstract
Persistent apical periodontitis represents a challenging clinical condition characterized by periapical lesions that remain unresolved despite conventional endodontic treatment. This condition constitutes a significant clinical problem associated with ongoing bone destruction, pain and treatment failure which may lead to extraction.This review aims to synthesize current understanding of the etiological factors underlying persistent apical periodontitis, examine clinical and radiographic features and evaluate contemporary and emerging therapeutic strategies for effective management.

I. Introduction

Endodontic infections involve complex polymicrobial communities thatflourish inside the root canal system. The conventional chemo-mechanical procedures often fall short in completely eliminating these microbes especially in cases where biofilm-forming and resistant bacteria are present(Fiegler-Rudol et al., 2025).

Apical periodontitis is a common inflammatory disease that is mainly caused by bacterial invasion and their byproducts which lead to the destruction of periapical tissues. Persistent apical periodontitis is a difficult situation in which periapical lesions remain even after multiple standard root canal treatments. Epidemiological data show that up to 52% of patientscan experience apical periodontitis in at least one tooth during their lifetime and in these cases approximately 4-15% may not resolve despite proper endodontic treatment(Li et al., 2026).

Persistent apical periodontitis is frequently associated with ongoing destruction of the periapical bone causing intense pain and eventual loss of function of the affected tooth(Nascimento et al., 2025, Petean et al., 2025). Moreover, the occurrence and severity of persistent apical periodontitis have been found to be higher in individuals with systemic conditions such as diabetes mellitus and coronary artery diseases which can be correlated to compromised immune function and changes in bone metabolism(Khalighinejad et al., 2016).

Persistent apical periodontitis can result from remaining microorganisms in treated root canals after intracanal disinfection procedures or secondary infections by microorganisms that are introduced into the root canals through breaches in the aseptic chain(da Silva et al., 2024).

Search strategy

An electronic search of articles from April 2019 to June 2019 was performed in two main databases: MEDLINE and the Embase Library. The search included only English-language publications with a focus on evidence-based research articles. A list of keywords was used with different combinations as follows: “persistent apical periodontitis,” or “persistent periapical periodontitis,”or “resistant endodontic infections”.

Causes of Persistent Apical Infections:

The microbiota linked to persistent apical infections generally have less diversity than primary endodontic infections but it comprises highly resilient microorganisms(Pérez-Carrasco et al., 2023).The presence of biofilms which isan extracellular matrix that adheres to the canal wallsand gives mechanical and chemical protection is important in persistent infections as it significantly reduces the efficacy of irrigants and disinfectants used during root canal therapy(Ricucci and Siqueira Jr, 2010) (Figure 1).

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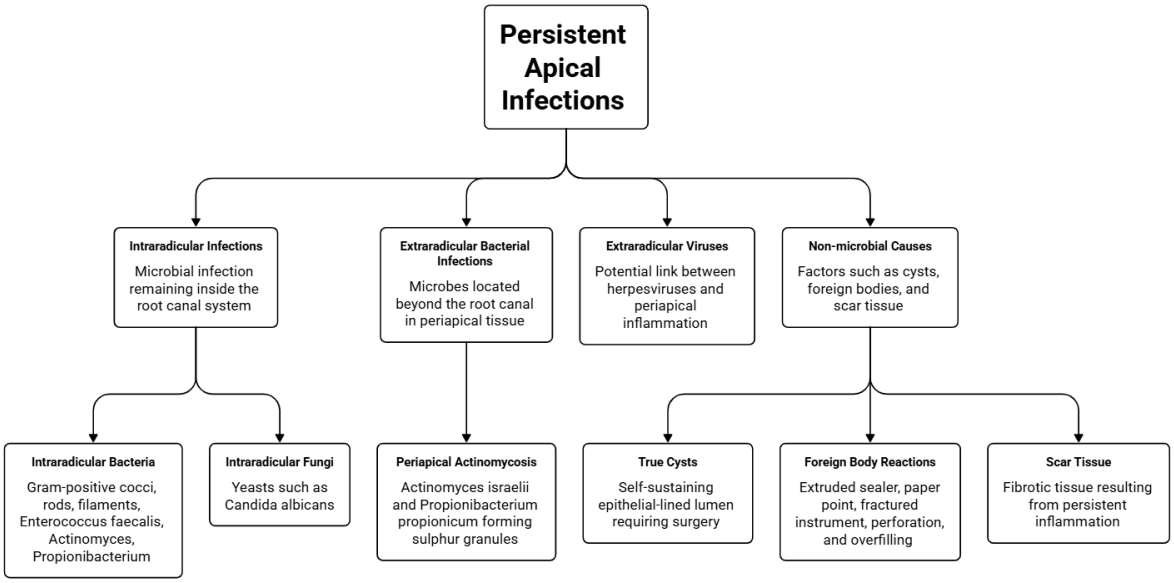

Figure 1:Causes of persistent apical infections.

1. Intraradicular Infections

Residual microbial infection remaining inside the complex apical root canal system is the major cause of persistent post-treatment apical periodontitis.Biofilm organization allowmicroorganisms to survive inside untouched anatomical spaces such as isthmuses and accessory canals by developing into protective sessile biofilms embedded in an extracellular matrix making them over 1000 times more resistant to treatment. Microorganismspersisting inside theroot canal can be most commonlybacteria or less commonly fungi(Nair, 2006, Pérez-Carrasco et al., 2023).

The persisting bacteria predominantly Gram-positive cocci, rods and filamentsare the common causes of persistent post-treatment apical periodontitis. The most frequently isolated and recalcitrant organism is *Enterococcus faecalis*which was found in 22% to 77% of cases. The ability to withstand a high pH up to 11.5, endure starvation and form monoinfections. Other common genera include *Actinomyces* and *Propionibacterium*. On the other hand, intraradicularfungi such as yeasts, specifically *Candida albicans* can persist within the canals and dentinal tubules, serving as a non-bacterial microbial cause of endodontic failure(Nair, 2006, Pérez-Carrasco et al., 2023).

2. ExtraradicularBacterial Infections

Microbes located beyond the root canal system inside the periapical tissue can initiate inflammation independently of the root canal.Periapical actinomycosis isa chronic granulomatous infection is caused by bacterial colonization in the periapical tissue primarily by *Actinomyces israelii* and *Propionibacterium propionicum*. These bacteria aggregate into structural, cohesive masses called sulphur granules colonies that successfully escape host defense mechanisms.*Propionibacterium propionicum* is also known to cause periapical infections and associated with actinomycotic infections. But the mechanism of pathogenicity of the organism has not yet been explained(Nair, 2006).

3. Extraradicular Viruses

Recent studies suggest a potential link between herpesviruses such as Cytomegalovirus or Epstein-Barr virus and inflamed periapical tissues, though it remains debated whether the virus causes the condition or is simply reactivated by the local inflammatory process(Nair, 2006).

Other Non-microbial Causes

Non-microbial causes of persistent apical periodontitis include cysts, foreign bodies, and scar tissue.True cysts represent a major non-microbial cause of endodontic failure because they possess a self-sustaining nature that allows them to grow independently of root canal infections. Cysts feature a lumen completely enclosed by an epithelial lining that is continuously growing. Because of thisthey fail to resolve with standard non-surgical retreatment and require surgical intervention to heal(Szaraz et al., 2025).

Periapical tissues frequently exhibit persistent inflammation due to foreign body reactions triggered by extruded dental materials and debris. Overextended gutta-percha, sealers, fractured instrument and perforationsometimesinduce intense localized macrophage responses. In addition

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cellulose materials like paper points and cotton wool resist cellular degradation(Nair, 2006, Ricucci et al., 2026).

Clinical and Radiographic Picture of Persistent Apical Infections:

An apical periodontitis lesion is expected to heal or significantly shrink within 6 months following a well-performed root canal treatment. However, the lesion isconsidered truly persistent if a periapical radiolucency remains completely unchanged, increases in size or emerges after treatment(Petean et al., 2025).

The radiographic pictures can vary according to severity of condition ranging from loss of apical lamina dura which may be partially or completely destroyed to large periapical radiolucency (Figure 2)(Suhail et al., 2026). The Periapical Index (PAI) is a standardized radiographic scoring system to evaluate the severity of apical periodontitis. It operates on an ordinal scale from 1 (healthy) to 5 (severe). The system relies on comparing a patient's periapical radiograph to a set of five validated reference radiographs that correspond directly to verified histological diagnoses(Venskutonis, 2016).

Figure 2: Radiographic picture of persistent apical infectionsafter 6 months with loss of apical lamina dura and obvious radiolucency around the mesial root of the first molar.

A wide spectrum of clinical signs and symptoms that vary based on whether the underlying inflammation is acute, chronic or asymptomatic(Petean et al., 2025).When the condition is symptomatic the primary complaint is pain localized to the affected tooth. Patients frequently experience pain during chewing or biting in addition to the sensation that the tooth is elongated in its socket. This occurs because inflammatory fluid accumulates at the apex physically elevating the tooth. During a clinical examination these cases demonstrate marked tenderness when the clinician taps on the tooth crown or presses against the alveolarmucosa overlying the root apex. Localized swelling in the adjacent mucosal tissue may also be visible if an acute abscess is forming(da Silva et al., 2024).

Conversely, asymptomatic presentations are often entirely painless and may only be discovered during routine radiographic monitoring. Despite the lack of pain, a classic clinical sign is the presence of a sinus tract sometimes may be seen. This acts as a drainage channel for chronic inflammatory exudate preventing pressure buildup. Periodontal probing should be done to check for any deep isolated pocket to differentiate between persistent apical periodontitis from a vertical root fracture or a combined endodontic-periodontal lesion(Siqueira Jr and Rôças, 2022).

Contemporary endodontic disinfection techniques for persistent apical infections:

In these cases, endodontic disinfection techniquesmainly depend on proper mechanical instrumentationin addition to chemical irrigants and intracanal medicaments(Gadzhula, 2016). While recent canal shaping systems have improved canal shaping, microbial elimination by these systems isinsufficient. The use of sodium hypochlorite as an irrigant and disinfectant was found to be unreliable in refractory cases. Although sodium hypochlorite is highly effective against a wide range of microorganisms and can dissolve organic tissue, its efficiency is confined by access as it may not be able to difficult areas such as lateral canals or apical ramifications (Siqueira Jr et al., 2007).

Enterococcus faecalis have been frequently found in obturated root canals exhibiting signs of chronic apical periodontitis. It was also cultured from periapical lesions that was found to be refractory to endodontic treatment. This is because it can deeply penetrate root dentinal tubules and forms strong, protective biofilms. E. faecalis can become resistant to sodium hypochlorite, hydrogen peroxide and ethanol (Kayaoglu et al., 2004, Gaeta et al., 2023).

Effective management of Enterococcus faecalis requires aggressive chemo-mechanical debridement. Proper mechanical instrumentation shapes the canals to strip away infected inner dentin layers. Utilizing chemical agents including sodium hypochlorite in high concentrations such as 5.25% rather than 2.5% and 17% EDTA to clean out the smear layer that may protect the bacteria. A final rinse with 2% chlorhexidine is recommended due to its substantivity and broad-spectrum activity. However, it is important to wash the canal properly from sodium hypochlorite to avoid the interaction between chlorhexidine and sodium hypochlorite which from a harmful brown precipitate known as

parachloroaniline which can be toxic and cause discoloration. Moreover, utilizing activation techniques using ultrasonic activation to enhance the penetration may enhance the penetration of these irrigants(Bui et al., 2008, Zou et al., 2024).

Choosing between retreatment or surgery

Evidence suggests that teeth with persistent apical infections and accessible coronal openings are suitable candidates for retreatment. Surgery may be the preferred option when retreatment is impossible due to limited coronal access or high risk of complications such as extensive restorations, fractured instruments, perforations, or ledges, teeth that have already undergone retreatment and cases requiring biopsy(Siqueira Jr and Rôças, 2022).

Innovative Strategies and Future Perspectives in management of persistent apical infections:

Current challenges in endodontic disinfection have sparked interest in alternative approaches that go beyond conventional chemical irrigants and medicaments.

Nanoparticle-based antimicrobials:

Nanoparticle-based antimicrobials are gaining significant interest because of their small size, large surface area, and ability to penetrate biofilms and dentinal tubules. Silver nanoparticlesshow broad-spectrum antimicrobial activity and have proven effective against E. faecalis biofilms without harming periapical tissues when used at appropriate concentrations. These particles work by disrupting microbial membranes which produce reactive oxygen species and interfering with cellular respiration. Research indicates that their effectiveness improves when combined with existing irrigants, although their long-term biocompatibility is still being studied(Bafail et al., 2025).

Common nanoparticles utilized in endodontics include silver nanoparticles which provide broad-spectrum bactericidal action especially against *E. faecalis* in endodontic infections(Praharsha et al., 2025). Calcium hydroxide nanoparticles enhance alkaline and antimicrobial dispersion compared to conventional micrometric pastes.In addition, chitosan nanoparticles offer natural, biocompatible, and biodegradable antimicrobial activity. Bioactive calcium-silicatenanoparticlesfunction has the ability to penetrate deeper into dentinal tubules in addition to their action against *E. faecalis* at depths up to 400 µminside the dentinal tubules(Afkhami et al., 2024). Another method is by utilizing oscillating magnetic fields. A helical nanobots equipped with an iron-cored silica blob-head are propelled to penetrate through dentinal tubules, while magnetic hyperthermia is employed to eradicate bacteria(Dasgupta et al., 2022).

Laser activated irrigation

For management of persistent apical infections,the erbium (Er)laser family is considered the most suitable for laser-activated irrigation which includeEr:YAG (2940 nm) and Er,Cr:YSGG (2780 nm). Erbium lasers have a high affinity for water and hydroxyapatite which enable strong activation effects and shock waves during irrigation.This induces rapid flow of the irrigant and high shear stress on the root canal walls. Moreover, lasers can generate reactive oxygen species that help destroy biofilms and directly promote bacterial death(Meire and De Moor, 2024).

A key advantage of erbium lasers is their remote bactericidal effect. However, the complex and variable anatomy of root canals can gradually reduce their optomechanical effectiveness from the coronal to the apical region(Zou et al., 2024). Photon-initiated photoacoustic streaming (PIPS) is another laser activation system derived from traditional erbium lasers. It operates by transmitting low-energy pulses (20–50 mJ) with extremely short durations (50 µs), producing sustained, intense shock waves that cause vigorous movement of irrigant within the canal. Studies have shown that PIPS enhances irrigant penetration into dentinal tubules and achieves superior disinfection compared to ultrasound(Peters et al., 2011). However, in vitro research indicates that a small amount of irrigant may extrude through the apical foramen and it remains unclear whether this could lead to postoperative pain in clinical settings. Additionally, laser-activated irrigation is not yet widely used in clinical practice due to the high cost of laser equipment(Zou et al., 2024).

Antimicrobial Photodynamic Therapy

Photodynamic therapyemploys a light-based method in which photosensitizing agents are activated by specific wavelengths to generate cytotoxic oxygen species that destroy microbial cells. This approach provides targeted antimicrobial effects with minimal damage to surrounding host tissues. This technique helps in disrupting mature biofilms, especially when used with conventional irrigation techniques. For example, methylene blue, a common photosensitizer, when activated by red light, can penetrate deep into the canal regions and significantly reduce viable bacterial populations. Both in vitro and clinical pilot studies support its role as an adjunct in root canal disinfection, although its effectiveness can vary depending on the microbial species involved and the specific application protocol (Bafail et al., 2025).

A recent systematic review and meta-analysis concluded that antimicrobial photodynamic therapy is highly effective at decreasing postoperative pain and reducing microbial loads when used as an adjunct to conventional root canal treatments. Additionally, by providing deep disinfection within dentinal tubules, the adjunctive therapy helps prevent secondary infections(Das et al., 2025). On the other hand, while photodynamic therapysignificantly decreases residual bacterial loads within the canal, it is ineffective at optimizing the elimination of bacterial endotoxins compared to conventional sodium hypochlorite irrigation(Barbosa et al., 2022).

Cold atmospheric plasma therapy

Cold atmospheric plasma (CAP) therapy has transitioned from biomedical research into endodontics which provide a non-thermal, gas-based approach capable of killing a broad spectrum of microbes. CAP produces a mixture of ions, electrons, and neutral particles that disrupt microbial DNA, proteins and cell membranes. In endodontic procedures, plasma jets can be directed into the root canal system to reach challenging areas. CAP demonstrates high antimicrobial effectiveness against biofilm-forming bacteria and fungi while remaining safe for surrounding tissues. Its low-temperature operation makes it suitable for delicate anatomical structures and ongoing advancements aim to improve delivery systems to ensure comprehensive coverage of the entire canal. CAP was found to be effective in preventing E. faecalis reinfection probably because of the plasma-generated reactive species which can successfully reach areas that are difficult to be reached by traditional antiseptics. (Sanesi et al., 2024).

Bacteriophage therapy

Bacteriophage therapy was traditionally studied in other infectious disease fields. Recently it been suggested for use in root canal disinfection. Bacteriophages are viruses that specifically infect and lyse bacteria, providing a highly targeted mode of action. Unlike broad-spectrum antimicrobials, phages do not disrupt the normal microbiota and can adapt to bacterial resistance through co-evolution with their hosts. Experimental studies indicate that phages targeting E. faecalis can significantly decrease biofilm biomass within dentinal tubules. Although their narrow host range can be a limitation in polymicrobial infections, it also reduces off-target effects. Currently, challenges related to delivery methods, formulation stability and regulatory approval hinder widespread clinical application. Nonetheless, phage therapy remains a promising avenue, particularly for retreatment cases or when resistant strains predominate the microbial community(Bafail et al., 2025).

II. Conclusion

Persistent apical periodontitis remains a challenging clinical condition that necessitates a thorough understanding of its complex etiology and pathogenesis. Recent advances in diagnostic techniquesand treatment modalities have enhanced our ability to effectively manage this condition. Recent innovations can offer promising prospects for improved healing and long-term tooth preservation.

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