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Infective endocarditis and oral health: a long-known threat, still a challenge

Mohamed Alsergani,[1] Renad Hatim Zaini,[2] Naji Al Kholaif,[3,4] Mohammed Al Admawi,[3] Maria Teresa Savo,[5] Dan Alexandru Cozac,[6] Donatella Tansella,[7] Basil Ali Aladani,[3] Sara Di Michele,[8] Valeria Pergola[5]

[1]Riyadh Elm University, Riyadh, Saudi Arabia; [2]Princess Nourah Bint Abdulrahman University, Riyadh, Saudi Arabia; [3]Heart Center of Excellence, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; [4]College of Medicine, Alfaisal University, Riyadh, Saudi Arabia; [5]Department of Cardiac, Thoracic and Vascular Sciences and Public Health, University of Padua, Italy; [6]Physiology Department, George Emil Palade University of Medicine, Pharmacy, Science and Technology of Târgu Mureș, Romania; [7]Division of Cardiology, Ospedale Mater Dei, Bari, Italy; [8]Division of Cardiology, San Filippo Neri Hospital, Rome, Italy

Abstract

Infective endocarditis (IE) remains a life-threatening condition associated with high morbidity and mortality, often influenced by the complex interplay between systemic and oral health. The increasing recognition of oral health as a risk modifier has led to greater focus on the oral microbiome, dental procedures, and periodontal disease as potential contributors to bacteremia and IE. This review critically examines the relationship between oral health and IE, exploring pathophysiological mechanisms, risk factors, and the evolving epidemiology of the disease.

The discussion includes diagnostic challenges, particularly in culture-negative cases, and the emerging role of advanced imaging and molecular diagnostics in improving early detection. A central focus is placed on preventive strategies, highlighting the debate surrounding antibiotic prophylaxis (AP) in high-risk individuals and the potential role of periodontal therapy in reducing systemic inflammation and transient bacteremia. The review also addresses the growing concern of antimicrobial resistance and the necessity of balancing AP recommendations with antimicrobial stewardship.

Additionally, this review identifies critical research gaps, including the need for longitudinal studies on the impact of oral health interventions on IE incidence and the importance of interdisciplinary collaboration between dental and medical professionals in optimizing patient care. By synthesizing current guidelines and emerging evidence, this review underscores the necessity of an integrated, multidisciplinary approach to mitigate the burden of IE and establish oral health as a key pillar of infection prevention.

Key words: infective endocarditis, antibiotic prophylaxis, oral microbiome, oral health.

Correspondence to: Maria Teresa Savo, Department of Cardiac, Thoracic and Vascular Sciences and Public Health, University of Padua, Via Giustiniani 2, 35128 Padua, Italy.
E-mail: mariateresa.savo@studenti.unipd.it

Introduction

Infective endocarditis (IE) is a life-threatening infection of the endocardial surfaces of the heart, primarily affecting heart valves and intracardiac devices. Despite advances in medical and surgical therapies, IE remains associated with high morbidity and mortality, particularly in patients with predisposing cardiac conditions [1-7]. Furthermore, the population at risk of IE has increased, and the clinical scenario has become even more challenging than in the past. The potential role of oral health in IE pathogenesis has gained increasing attention due to the ability of oral bacteria to enter the bloodstream, leading to bacterial adhesion and biofilm formation on damaged endocardial tissue [1-11]. The oral cavity harbors a diverse microbiome, including *Streptococcus mutans*, *Streptococcus sanguinis*, and *Porphyromonas gingivalis*, which can translocate into the bloodstream during routine activities such as chewing or toothbrushing, as well as during invasive dental procedures [9-14]. While the immune system and endothelial integrity usually prevent bacterial colonization, individuals with prosthetic valves, congenital heart disease (CHD), or a history of IE are at particularly high risk for bacterial seeding and vegetation formation [1]. Once oral bacteria adhere to damaged heart valves, they form biofilms, which provide protection from immune defenses and antimicrobial therapy, making IE difficult to eradicate [1-11].

This review aims to synthesize and critically analyze the current evidence on the relationship between oral health and IE, with a focus on diagnostic advancements, prevention strategies, and management approaches. By addressing discrepancies in international guidelines on antibiotic prophylaxis (AP), evaluating the impact of periodontal therapy on bacteremia reduction, and discussing the emerging challenges posed by antimicrobial

resistance (AMR), this review highlights the need for an interdisciplinary approach to mitigate the global burden of IE.

Epidemiology and etiology of infective endocarditis

IE is a multifactorial disease whose estimated incidence in 2019 was 13.8 cases per 100,000 subjects per year [1,8]. According to the Euro-Endo registry, IE predominantly affects men around 60 years of age [3]. In developed countries, *Staphylococcus Aureus* has surpassed viridans group streptococci (VGS) as the leading causative pathogen, accounting for up to 44% of cases [1-8]. Other frequently implicated bacteria include enterococci, oral streptococci, and *Streptococcus gallolyticus*. According to the results of the Euro-Endo registry [2], the most frequent microorganisms involved were staphylococci in 1085 (44.1%) patients, followed by enterococci in 390 (15.8%), oral streptococci in 304 (12.3%), and *Streptococcus gallolyticus* in 162 (6.6%) patients [3].

Oral pathogens, particularly VGS such as *Streptococcus mitis* and *Streptococcus sanguinis* [1,9-23], as well as periodontal pathogens like *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, have been implicated in IE pathogenesis [1-23]. While dental procedures are a well-recognized source of bacteremia, even everyday oral hygiene activities have been found to be able to induce transient bacteremia, especially in individuals with poor periodontal health [1,8-23].

According to the Euro-Endo Registry from the European Society of Cardiology (ESC) [2], dental procedures were among the most frequently reported non-cardiac interventions preceding IE. The most common portals of entry for IE were: oral/dental sources (9.8%), digestive tract infections (6.3%), and genitourinary tract infections (4.5%) [3]. Notably, the proportion of oral streptococcal IE cases has decreased over time, with the lower prevalence reported in the Euro-Endo Registry (12.4%) compared to previous studies [2], including the EuroHeart Survey (15%) [5], the 2002 French Registry (20.6%) [6], and the International Collaboration on Endocarditis-Prospective Cohort Study (17%) [7].

These findings underscore the importance of maintaining optimal oral health, particularly in high- and intermediate-risk populations, as a means of reducing transient bacteremia and preventing IE. In addition to guideline-based AP, improving periodontal health and routine dental care may represent a crucial strategy to mitigate the risk of oral pathogen-induced IE.

Role of the oral microbiome in infective endocarditis pathogenesis

The oral microbiome consists of over 700 bacterial species, many of which contribute to both oral and systemic health when in balance [8-23]. However, when dysbiosis occurs, an imbalance in microbial composition, the risk of periodontal disease, dental infections, and systemic bacteremia increases. Disruptions in the oral microbiome have been implicated in the development of IE due to the translocation of bacteria into the bloodstream, which can result in bacterial adhesion to the endocardium and biofilm formation on damaged heart valves [11].

Dental caries and periapical infections

Microbial changes and the pathogenesis of dental caries

Dental caries is a biofilm-mediated infectious disease that results from the imbalance between demineralization and remineralization of dental hard tissues due to acidic bacterial by-products. The process begins when dietary carbohydrates, particularly fermentable sugars, lead to a shift in microbial composition, favoring the proliferation of acid-producing bacteria, such as *Streptococcus mutans* and *Lactobacillus* species [8,9,11].

When the oral biofilm becomes dominated by acidogenic bacteria, the lowered pH within the biofilm disrupts the protective enamel layer, promoting dental decay. This dysbiotic shift results in the breakdown of enamel, dentin, and cementum, allowing bacteria to invade deeper tooth structures [8,9,11]. Some bacteria enhance acid buffering, while others accelerate biofilm acidity, influencing the rate of enamel breakdown [8,9,11]. The extent of caries formation is also multifactorial, influenced by salivary composition, which affects acid neutralization and enamel remineralization; genetic factors, which determine enamel strength and immune responses; dietary habits, particularly the frequency of carbohydrate intake; and oral hygiene practices, which influence plaque accumulation and microbial load [8,9,11].

Progression to periapical infections

When dental caries progresses, they penetrate beyond the enamel into the pulp chamber, resulting in pulpal inflammation (pulpitis). If untreated, this condition can advance to pulp necrosis, allowing bacteria to spread into the periapical tissues, periodontal ligament, and alveolar bone [8,9,12]. Inflammation and immune reactions in the periapical tissue cause resorption of the surrounding bone, detected as a radiolucent area on X-ray imaging [24].

Periapical infections are polymicrobial in nature, typically involving 10-20 different bacterial species, including Gram-negative anaerobes such as *Fusobacterium nucleatum* and *Prevotella intermedia*. However, when previously treated teeth develop recurrent infections, the bacterial diversity decreases, with Gram-positive species such as *Staphylococcus* and *Enterococcus* becoming predominant [8,9,11,13].

These infections may remain chronic and asymptomatic, allowing for silent bacterial dissemination, increasing the risk of transient bacteremia and potential IE development in at-risk individuals. In line with the ALARA principle ("As Low As Reasonably Achievable"), we believe that radiographic examinations should be considered only when there is a well-founded clinical suspicion of odontogenic infection, rather than as part of a routine screening protocol, even in patients at high risk for IE.

Periodontal disease and its systemic implications

Microbial dysbiosis and periodontitis development

Periodontal disease is a chronic inflammatory condition affecting the tooth-supporting structures, including the gingiva, periodontal ligament, and alveolar bone. The transition from a healthy subgingival microbiome to a dysbiotic microbial community drives dis-

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ease progression, leading to irreversible attachment loss, increased pocket depth, and eventual tooth mobility [8,9,15,16,20].

While historically attributed to specific anaerobic bacteria, such as *Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola*, and *Aggregatibacter actinomycetemcomitans*, recent metagenomic studies suggest that periodontitis arises from complex polymicrobial interactions. The dysbiotic shift activates host immune responses, leading to the release of pro-inflammatory cytokines, which contribute to systemic inflammation and tissue destruction [8,9,15,16,20].

Bacteremia and endocarditis risk from periodontal disease

Periodontal disease significantly increases the risk of transient and sustained bacteremia, particularly during chewing, tooth brushing, and dental procedures [8-9,15-16,20]. This oral bacterial translocation is a well-documented risk factor for IE in susceptible individuals, particularly those with valvular disease, prosthetic heart valves, or previous IE episodes.

Due to the high bacterial load in periodontal pockets, periodontitis is a major source of bacteremia-associated endocarditis. Studies have demonstrated that patients with untreated periodontal disease exhibit elevated levels of C-reactive protein (CRP) and pro-inflammatory cytokines, suggesting a systemic inflammatory burden that could contribute to IE development [16,20].

Dental procedures, bacteremia, and infective endocarditis

Because odontogenic infections harbor a high bacterial load, gingival trauma and invasive procedures may facilitate the entry of bacteria into the bloodstream, causing transient bacteremia [1-4]. Sources of dental-associated bacteremia in dental procedures are shown in Table 1.

Oral bacteria and molecular links to infective endocarditis

Among the diverse microbial species implicated in IE, VGS remain one of the most significant contributors, particularly in individuals with underlying cardiac abnormalities. Other species, such as *Streptococcus sinensis*, rely on their potential to cause severe infections, particularly in immunocompromised individuals or those with predisposing risk factors [18].

Recent genomic studies have further elucidated the molecular mechanisms by which oral bacteria interact with systemic host defenses, including biofilm formation, immune evasion, and endothelial adhesion [19].

Given the growing evidence linking oral dysbiosis to systemic diseases, including IE, the maintenance of oral health is increasingly recognized as a critical factor in preventing bacteremia-related infections.

Oral health as a risk modifier

The importance of oral hygiene as a preventive measure for IE is increasingly recognized. Studies have demonstrated a strong correlation between poor oral health and increased risk of IE, particularly in individuals with high dental plaque and calculus indices [20].

Chronic periodontitis not only facilitates bacterial translocation but also exacerbates systemic inflammation, contributing to diabetes, cardiovascular disease, and endothelial dysfunction, all of which are established risk factors for IE. Professional dental care has been shown to reduce systemic inflammatory markers, such as CRP and interleukin-6, further reinforcing the broader systemic benefits of maintaining optimal oral health [8,9,16].

The latest ESC guidelines for IE prevention emphasize the importance of daily oral hygiene and regular professional dental care, particularly for high-risk populations [1]. These guidelines recommend: i) brushing teeth twice daily with fluoride toothpaste; ii) professional dental cleaning at least twice a year for high-risk individuals and annually for others; iii) strict skin and wound hygiene, particularly in individuals with cardiac implants or prosthetic valves; iv) targeted antibiotic treatment for bacterial infections in high-risk patients following blood culture results; v) avoidance of self-medication with antibiotics, which contributes to AMR; vi) minimization of invasive procedures, particularly tattooing, piercings, and unnecessary infusion catheter placements, which have been identified as potential entry sites for bacterial infection [1].

Diagnostic approaches for infective endocarditis

The diagnosis of IE relies on a combination of clinical suspicion, microbiological analysis, and imaging techniques. The modified Duke and ESC guidelines criteria remain the cornerstone of IE diagnosis, incorporating major criteria such as positive blood cultures and imaging evidence of endocardial involvement [1-8,25-27] with minor criteria. Blood cultures drawn before initiating antibiotic therapy to maximize diagnostic yield and improve pathogen identification have been given a class 1 of recommendation in both America Heart Association (AHA) and ESC guidelines [1,4]. Notably, not only patients with definite IE but also, according to the AHA, with a red-flagged 3 harm recommendation, all valvular heart disease patients with unexplained fever should not receive antibiotics without blood culture.

Table 1. Sources of bacteremia in dental and oral procedures.

Category	Specific procedures/activities	Potential risk
Invasive dental procedures	Tooth extractions; periodontal and apical surgery; subgingival caries removal; dental prophylaxis; non-surgical periodontal therapy	Direct introduction of oral bacteria into the bloodstream
Endodontic treatments	Root canal treatments; instrumentation of periapical region	Release of bacteria into circulation due to deep tissue manipulation
Routine oral activities	Chewing; flossing; tooth brushing	Transient bacteremia, particularly in individuals with gingival inflammation

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Advances in molecular diagnostics

Emerging molecular techniques, such as polymerase chain reaction (PCR) and metagenomic sequencing, are increasingly used as adjunctive diagnostic tools, particularly in cases of culture-negative IE. These methods allow for the direct detection of causative organisms from clinical specimens, improving diagnostic accuracy when conventional blood cultures fail to identify the pathogen [1,4].

Role of advanced imaging modalities

Nowadays, the IE imaging arena has been expanded, and novel imaging techniques have been recognized as major criteria [1,4]. Imaging plays a pivotal role in the diagnosis, risk stratification, and management of IE, providing crucial insights into the extent of valvular and extracardiac involvement. Therefore, a comprehensive, multimodality imaging approach is essential for improving the diagnostic accuracy and management of IE. Echocardiography remains the first-line modality, with the transthoracic approach serving as an initial screening tool and transesophageal echocardiography (TEE) offering superior sensitivity, particularly for detecting small vegetations, perivalvular abscesses, complex anatomic morpho-pathologies such as pseudoaneurysm, fistulas, valvular aneurysm, and prosthetic valve involvement. 3D TEE has further enhanced the evaluation of complex valvular and perivalvular lesions and the assessment of embolic potential by offering more precise vegetation size assessment and spatial resolution [28].

Beyond echocardiography, advanced multimodality imaging techniques have become essential in cases where echocardiographic findings are inconclusive or when further characterization of complications, in particular perivalvular lesions, is needed. Cardiac computed tomography (CT) provides detailed anatomical information, particularly useful in assessing prosthetic valve complications, perivalvular abscesses, and embolic events. Positron emission tomography-CT (PET-CT) with fluorodeoxyglucose has emerged as a powerful tool for detecting low-grade infections and prosthetic valve endocarditis by identifying increased metabolic activity in infected tissues. PET-CT is especially valuable in cases of culture-negative IE and in differentiating active infection from non-infectious postoperative changes in prosthetic valves. According to the latest ESC guidelines, PET-CT is now considered a major criterion for detecting prosthetic valve infections and extracardiac embolic complications, particularly in patients with suspected but culture-negative IE [1]. Moreover, PET-CT may be considered in possible cardiac device-related IE to confirm the diagnosis. The incorporation of multimodal imaging into diagnostic pathways enhances early detection and guides treatment strategies, particularly in complex cases (Figure 1).

Magnetic resonance imaging plays a complementary role, particularly in the detection of cerebral complications, such as silent embolic infarcts, microbleeds, and mycotic aneurysms, which have prognostic implications and represent minor criteria for the diagnosis. Whole-body imaging techniques also aid in identifying extracar-

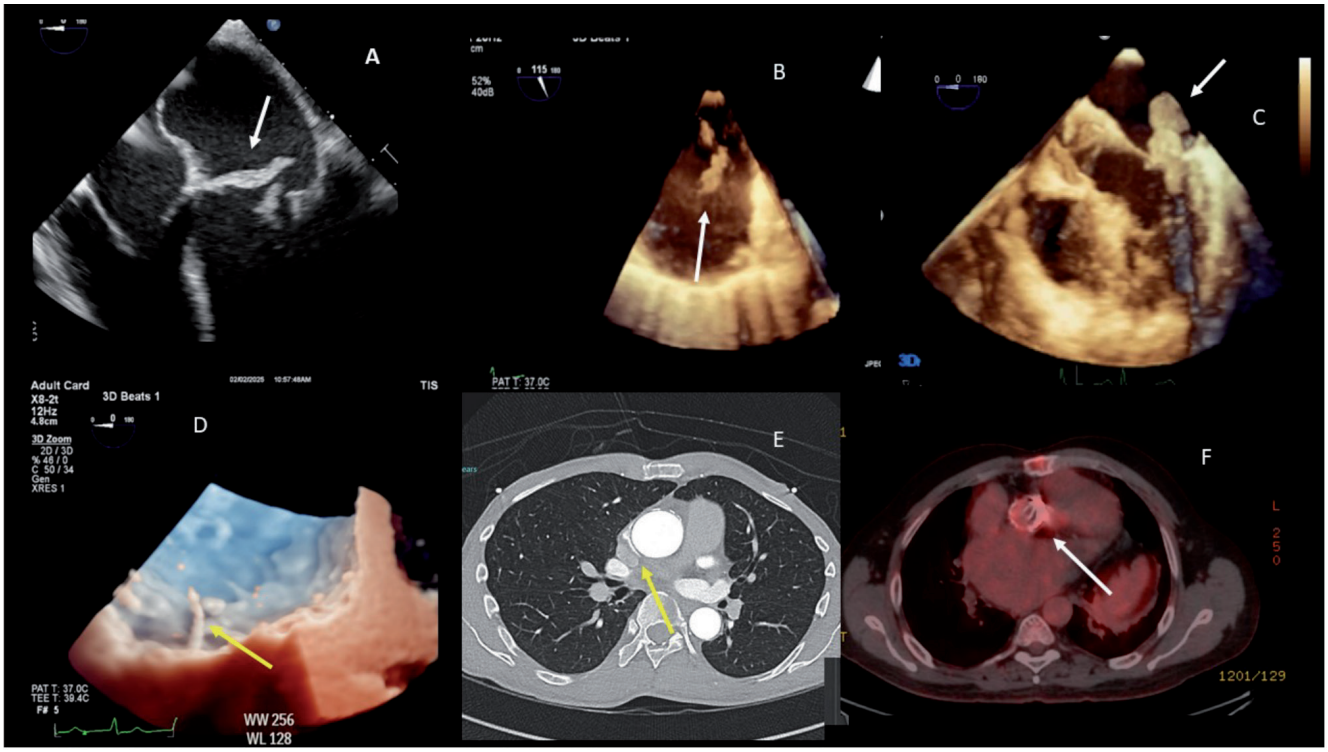


Figure 1. Multimodality imaging in infective endocarditis. A) 2D transesophageal echocardiography (TEE): 4-chamber esophageal view – large vegetation attached to the base of the anterior mitral leaflet in a patient affected by Staphylococcus aureus infective endocarditis; B) 3D TEE: surgical right atrial view – large vegetation attached to the Eustachian valve; C) 3D TEE: huge vegetation attached to the posterior mitral leaflet in a patient affected by Staphylococcus aureus infective endocarditis; D) 3D TEE: surgical left atrial view, large vegetation attached to the atrial surface of mechanical prosthetic mitral valve; E) cardiac computed tomography, short axis view at the level of the aorta showing a small pseudoaneurysm (arrow) posterior to the aortic root; F) fluorodeoxyglucose uptake in the aortic wall at combined positron emission tomography/computed tomography corresponding to infectious endocarditis.

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diac infectious foci, including septic emboli to the spleen, kidneys, and musculoskeletal system.

Antibiotic prophylaxis and its evolving role

The role of AP in preventing IE has been widely debated over the years. Currently, no prospective randomized trial exists, but only retrospective and observational studies. Due to the lack of supporting evidence, in 2008, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom for the National Health Service recommended cessation of AP for dental procedures in all people at risk for IE [29]. By contrast, the AHA and the ESC produced new guidelines in 2007 and 2009, respectively, recommending cessation of AP for patients at moderate risk only [30,31]. A major challenge, and source of ongoing confusion, in evaluating data on IE AP lies in several compounding factors. The low incidence of IE necessitates very large cohorts to reach statistical significance. Additionally, the wide variability in the type and severity of underlying cardiac conditions requires large, well-matched control groups for each specific condition. Finally, the broad range of invasive dental procedures and dental disease presentations makes it difficult to standardize exposure groups, further complicating interpretation and comparison across studies. These and other limitations complicate the interpretation of the results of published studies of the efficacy of IE prophylaxis in patients who undergo dental procedures. After the NICE recommendation introduction, prescriptions of AP have fallen substantially (about 88%), and the incidence of IE has increased significantly in England [32]. This increase was over and above what would have been expected from projection of the background pre-NICE upward trend in IE incidence and suggested that by March 2013 there were an extra 419 IE cases per year than expected. The 95% confidence limits suggested this figure could be as high as 743 or as low as 117 extra cases [32]. These data raised the possibility that the NICE guidance was causing an increase in the number of IE cases and led NICE to announce a review of its guidance.

After that, NICE and the ESC announced the results of their own reviews after reevaluation of exactly the same evidence. NICE announced that there was insufficient evidence to warrant any change to their existing guidance not to recommend AP. At the same time, the ESC concluded that the weight of evidence and opinion was in favor of the efficacy and usefulness of AP in preventing IE in high-risk patients. They also concluded that the risk of not giving AP outweighed any risk of giving it and therefore recommended that AP should be given before invasive dental procedures to all patients at high-risk of IE. Moreover, the ESC guideline committee acknowledged but ultimately rejected the NICE position, emphasizing the poorer prognosis of IE in high-risk individuals, particularly those with prosthetic valves, and highlighted that these high-risk patients represent only a small fraction of those who previously received AP. This, in turn, would significantly limit the number of individuals exposed to potential adverse effects of AP. The AHA guidelines agreed with the ESC guidelines. A further analysis by the British Dental Association published in 2016 suggests that, based on available data published in The Lancet [32], the potential risk associated with implementing the NICE guidance, which recommends no AP, could result in an estimated 419 additional cases of IE per year in the UK, potentially including up to 66 additional deaths annually. In contrast, following the ESC guidance, which recommends AP in high-risk patients, might lead to only around seven reportable adverse drug reactions annually, including 1 death every 3 years. Moreover, if amoxicillin were used exclusively for AP, or a safer alternative to clindamycin were adopted, this number could be reduced to just two reportable adverse reactions per year. These projections indicate that, pending new evidence, the ESC approach may present a safer overall strategy for most patients compared to the current NICE guidance [33].

In 2018, a document by a group of experts in the prevention and treatment of IE was released, dealing with morbidity or mortality from VGS IE after publication of the 2007 guidelines, and 18 trials were reviewed. The results showed that there was no evidence that VGS IE frequency, morbidity, or mortality has increased since 2007. There is no convincing evidence from retrospective and observational studies that there was an increase in frequency of and morbidity or mortality from VGS IE since 2007 in the 4 high-risk groups defined in the 2007 guidelines. As limitations, we have to consider the small number of cases of VGS IE that could be prevented by AP for a dental procedure. Nonetheless, even though the effectiveness of such prophylaxis has not been demonstrated, this approach has been believed safer and able to reduce the uncertainties due to the lack of reliable trials for patients at high risk. The last AHA and ESC guidelines suggest AP prior to dental procedures that involve manipulation of gingival tissues, the periapical region of the teeth, or perforation of the oral mucosa for patients with valvular heart disease who are at increased risk for IE [1,4]. American guidelines did not differentiate between high and intermediate risk of IE. In contrast, more recent ESC guidelines have introduced this distinction, promoting a more stratified approach to AP based on individual risk levels. According to the latest ESC guidelines, patients can be classified into high-risk and intermediate-risk groups of IE, guiding the use of AP [1] (Table 2).

High-risk patients, in whom AP is recommended, include those with a history of IE; prosthetic heart valves, including surgically or transcatheter-implanted valves; any cardiac material used for valve repair; CHD requiring surgical intervention; ventricular assist devices. In particular, patients with prosthetic valve endocarditis

Table 2. International guidelines on antibiotic prophylaxis for infective endocarditis.

Guideline/Organization	Recommendation	Primary concern
American Heart Association (AHA) 2021	Prophylaxis for high-risk individuals undergoing invasive dental procedures	Prevention of IE in prosthetic valve and IE-history patients
European Society of Cardiology 2023	Similar to AHA—supports prophylaxis for high-risk cases	Consistency with risk stratification
National Institute for Health and Care Excellence 2008	Discontinued routine prophylaxis for all patients	Antimicrobial resistance concerns

IE, infective endocarditis.

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have an in-hospital mortality rate that is twice as high with more complications as compared with patients with native valve endocarditis. Furthermore, mitral and aortic bio-prostheses may be associated with increased risk of IE as compared with mechanical prostheses [1,34,35]. Patients with septal defect closure devices, left atrial appendage closure devices, vascular grafts, vena cava filters, and central venous system ventriculo-atrial shunts are considered within this risk category in the first 6 months after implantation [1,4,36]. The criteria defining high-risk patients are largely shared between AHA, ESC, and Dentistry guidelines [1,4,37].

Intermediate-risk patients, in whom AP is not routinely recommended and may be considered, include individuals with rheumatic heart disease; non-rheumatic degenerative valve disease; congenital valve abnormalities, such as bicuspid aortic valve; cardiovascular implantable electronic devices; hypertrophic cardiomyopathy [1].

Current guidelines on antibiotic prophylaxis

Recent studies suggest that AP, when combined with optimal oral hygiene, significantly reduces IE incidence in high-risk patients. First-line prophylactic regimens typically include amoxicillin and ampicillin and cephazolin or ceftriaxone, with azithromycin, clarithromycin, or doxicilina recommended for penicillin-allergic individuals [1] (Table 3).

Antimicrobial resistance: a growing concern

The overuse of antibiotics, including prophylactic regimens, has led to the emergence of multidrug-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci. These resistant organisms complicate the treatment of IE, often necessitating the use of combination antibiotic therapy or newer antimicrobial agents [1,4,9,17,21,23].

To combat rising resistance rates, antimicrobial stewardship programs emphasize: i) judicious antibiotic use, reserving AP only for high-risk patients; ii) targeted therapy based on blood cultures, rather than empirical broad-spectrum regimens; iii) exploration of alternative antimicrobial strategies, such as bacteriophage therapy and antimicrobial peptides, which show promise in overcoming resistance [1,4,9-23].

Periodontal therapy and preventive measures

Non-surgical periodontal therapy, including scaling and root planing, has been shown to reduce microbial load and systemic inflammation, potentially lowering bacteremia-associated risks. Regular dental check-ups and patient education on oral hygiene practices are critical components of preventive care.

Integration of periodontal care into cardiovascular health

Emerging evidence supports the inclusion of dental assessments in cardiovascular risk stratification models. Given the link between periodontal disease, systemic inflammation, and cardiovascular pathology, comprehensive periodontal care should be considered a complementary strategy in reducing systemic infection risks [24]. Furthermore, to operationalize the integration of dental and cardiovascular care, several strategies have been proposed. These include the implementation of shared electronic health records to facilitate communication between dental and medical providers [38], the establishment of joint multidisciplinary clinics for co-management of high-risk patients, and the development of interprofessional education programs to enhance collaborative understanding and referral practices [8]. Such models aim to bridge the gap between oral and systemic health, promoting more effective prevention and management of IE. Recently, in some hospitals, a dedicated inpatient cardiac dental clinic has been established to enhance awareness and provide targeted education for patients of all ages who are either diagnosed with or at high risk of developing IE. This initiative is complemented by a structured oral health education program integrated into specialized valve outpatient clinics. Providing professional oral hygiene support alongside behavioral interventions has shown promise in improving oral health outcomes in this population.

Management of infective endocarditis linked to oral pathogens

The management of IE caused by oral pathogens requires a multidisciplinary approach, involving infectious disease specialists, cardiologists, and dental professionals. Early diagnosis and prompt intervention are critical to reducing morbidity and mortality associated with bacteremia and IE.

Antibiotic therapy for oral pathogen-related infective endocarditis

The initial treatment of IE caused by oral pathogens, particularly VGS and periodontal bacteria, consists of targeted intravenous antibiotic therapy guided by microbiological cultures and susceptibility testing. Combination antibiotic regimens, typically including beta-lactams (*e.g.*, penicillins, cephalosporins) and aminoglycosides (*e.g.*, gentamicin), are commonly employed in oral streptococcal IE [1]. The recommended standard antibiotic treatment for IE linked to oral streptococci includes Penicillin G, amoxicillin, or ceftriaxone, recommended for 4 or 6 weeks (respectively in native and prosthetic valve endocarditis). In cases of penicillin resistance, aminoglycoside therapy, such as gentamicin, should be administered for a minimum of 2 weeks. For patients with a documented penicillin allergy, desensitization is the preferred approach. However, if desensitization is not feasible, alternative treatments should be selected based on the severity of the allergic reaction.

For non-anaphylactic penicillin allergies, cephalosporins are a viable option. In contrast, patients with a history of anaphylactic reactions to beta-lactams should receive vancomycin as the preferred alternative.

In cases involving highly virulent organisms, such as *Staphylococcus aureus* or *Porphyromonas gingivalis*, more aggressive regimens have been recommended [1,4].

Table 3. Preferred antibiotics for infective endocarditis prophylaxis (European Society of Cardiology guidelines).

Patient group	Preferred antibiotics	Dosage
No penicillin allergy	Amoxicillin, ampicillin, cefazolin, ceftriaxone	2 g orally, 30-60 minutes before procedure
Penicillin allergy	Azithromycin, clindamycin	500 mg orally (azithromycin), 600 mg orally (clindamycin)

Surgical intervention in complicated infective endocarditis

Surgical intervention is indicated in cases of heart failure primarily due to valve dysfunction, uncontrolled infection, and high risk of embolization due to large vegetation [1,3,4]. Early surgical referral has been found to be particularly important in all the above settings: i) persistent infection despite appropriate antibiotic therapy (fever and bacteremia lasting >7 days); ii) large (>10 mm) or mobile vegetations with a high risk of embolism; iii) severe valvular damage, leading to acute heart failure; iv) local complications such as perivalvular abscess formation, fistula development, false aneurysm, and enlarging vegetation [1,4].

Research gaps and future directions

Despite substantial advancements in understanding the interplay between oral health and IE, several critical gaps remain that warrant further investigation. One of the most pressing issues is the need for longitudinal studies to establish causality between oral health and IE risk. While cross-sectional studies have consistently demonstrated an association between poor oral hygiene and increased IE incidence, long-term prospective research is necessary to determine whether improving oral health directly reduces IE occurrence in high-risk populations.

Another key area for future research is the advancement of molecular diagnostics for early IE detection. Traditional blood cultures, though widely used, often fail to identify causative pathogens in cases of culture-negative IE, leading to diagnostic delays and suboptimal treatment. The integration of next-generation sequencing, metagenomic approaches, and PCR-based assays has shown promise in identifying pathogens more rapidly and accurately. However, further studies are required to assess the feasibility, cost-effectiveness, and clinical utility of these cutting-edge diagnostic tools in routine medical practice.

A major challenge in IE prevention lies in balancing antibiotic prophylaxis with the growing threat of AMR. While AP use has been recommended for high-risk individuals undergoing invasive dental procedures, concerns over antibiotic overuse and resistance development have led to revisions in guideline recommendations. Future strategies should focus on personalized risk stratification, allowing for targeted AP in individuals who would benefit most, while minimizing unnecessary antibiotic exposure.

Finally, there is a growing need to strengthen the integration of dental and cardiovascular care models to enhance IE prevention efforts. While dental health and cardiovascular risk are often managed separately, the evidence linking periodontal disease to systemic inflammation and cardiovascular complications suggests that a more interdisciplinary approach is warranted. Future research should evaluate the impact of routine dental screening and periodontal therapy in patients with underlying cardiac conditions, particularly those at elevated risk for IE.

Conclusions

IE remains a serious clinical and public health challenge, requiring multifaceted prevention and management approaches. A patient-centered approach is crucial. This involves tailoring diagnostic strategies to the individual's specific condition, clinical presentation, and history, rather than applying a one-size-fits-all multimodal approach [39]. This review underscores the critical role of oral health in reducing IE risk, particularly in high-risk populations.

While AP remains a subject of ongoing debate, maintaining optimal oral hygiene and periodontal care has emerged as a universally recognized preventive strategy. Future research should focus on harmonizing conflicting guidelines, advancing diagnostic technologies, and refining prophylactic and therapeutic interventions.

An interdisciplinary approach, integrating dental professionals, cardiologists, and infectious disease specialists, is pivotal in reducing the burden of IE and improving patient outcomes. By fostering collaboration between oral and systemic health disciplines, the risk of IE can be significantly mitigated, reinforcing the importance of a comprehensive, evidence-based approach to infection prevention.

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