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The Oral–Systemic Inflammation Axis: Integrating Dental Assisting, Hematological Biomarkers, Laboratory Diagnostics, Pharmacological Interventions, and Physical Rehabilitation.

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Abstract

Periodontitis and related oral infections are increasingly recognized as modifiable contributors to systemic inflammation, with consequences for cardiometabolic, respiratory, and immune health. This narrative review synthesizes literature published between 2017 and 2025 on the oral–systemic inflammation axis and integrates the contributions of seven health disciplines: laboratory medicine, dental assisting, nursing, medical genetics, pharmacy, hematology, and physical therapy. Mechanistic evidence indicates that dysbiotic biofilms, neutrophil and monocyte dysregulation, oxidative stress, and cytokine spillover link oral inflammation with systemic disease. Biomarkers such as C-reactive protein, interleukin-6, and blood-cell ratios offer accessible monitoring tools, while genetic variation modulates susceptibility. Mechanical biofilm control, rational antimicrobial and anti-inflammatory prescribing, nursing surveillance, and structured exercise each demonstrate measurable effects on inflammatory burden. We propose an integrated interprofessional framework, identify evidence gaps, and outline priorities for standardized biomarker panels and collaborative care pathways.

Keywords: oral–systemic axis; periodontitis; inflammatory biomarkers; interprofessional care; exercise.

Introduction

The mouth has long been treated as an anatomically and professionally separate territory from the rest of the body. Contemporary immunology and epidemiology have steadily dismantled that separation. Periodontal diseases, which comprise the gingival inflammation of gingivitis and the destructive, biofilm-driven inflammation of periodontitis, are among the most prevalent chronic inflammatory conditions worldwide and a leading cause of tooth loss in adults (Kinane et al., 2017). Because the periodontium is a highly vascularized tissue in constant contact with a polymicrobial biofilm, the oral cavity offers a continuous route through which microbial products, inflammatory mediators, and activated immune cells can reach the circulation (Hajishengallis, 2022). Periodontitis is therefore best conceptualized not merely as a local disease of the tooth-supporting tissues but as a source and amplifier of low-grade systemic inflammation.

This conceptual shift coincides with a broader reappraisal of chronic inflammation as a unifying driver of age-related and non-communicable disease. Persistent, sterile, low-grade inflammation contributes to atherosclerosis, type 2 diabetes, neurodegeneration, frailty, and cancer, and it accumulates across the life span through the interplay of genetic, behavioral, microbial, and environmental exposures (Furman et al., 2019). Within this framework, the oral cavity represents an unusually accessible and treatable inflammatory focus. Unlike many other contributors to systemic inflammation, periodontal inflammation can be visualized,

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measured, staged, and reduced by well-defined clinical interventions.

The classification of periodontal conditions has also matured. The 2017 World Workshop framework redefined periodontal health, gingivitis, and periodontitis using staging and grading that reflect disease severity, complexity, rate of progression, and systemic risk modifiers (Chapple et al., 2018; Tonetti et al., 2018). This framework explicitly acknowledges that the patient's systemic status, including glycemic control and smoking, shapes the periodontal phenotype, and that periodontal status in turn may influence systemic health. Consensus reports have since examined the evidence connecting periodontitis with cardiovascular disease, diabetes, and respiratory disease, concluding that associations are consistent and biologically plausible, although causal evidence of benefit from periodontal therapy on hard systemic outcomes remains incomplete (Herrera et al., 2023; Sanz et al., 2020a). Reviews of the field emphasize that the relationship is bidirectional and multifactorial rather than linear (Martínez-García & Hernández-Lemus, 2021).

Translating this knowledge into practice demands more than dentistry alone. Detection of systemic inflammatory burden relies on laboratory diagnostics and hematological indices. Susceptibility is shaped by inherited variation that medical genetics is beginning to characterize. Control of inflammation involves mechanical, antimicrobial, and anti-inflammatory strategies managed with pharmacists. Patient monitoring and education are core nursing functions, and exercise prescribed by physical therapists influences systemic immune signaling. Dental assistants, positioned at the interface of daily clinical operations, perform much of the preventive and infection-control work that sustains oral health. Despite this natural convergence, the literature on each discipline is typically siloed.

The aim of this narrative review is to integrate evidence from these seven domains into a coherent model of the oral–systemic inflammation axis. Specifically, we (a) summarize the mechanistic basis of the axis, (b) describe laboratory and hematological markers used to quantify inflammation, (c) outline genetic contributions to susceptibility, (d) examine the roles of dental assisting, nursing, pharmacy, and physical therapy in modulating inflammatory burden, and (e) propose an interprofessional framework and research agenda.

2. Review Approach

This work follows a narrative, rather than systematic, design, which is appropriate for synthesizing heterogeneous evidence across several professions and for building conceptual frameworks. Literature published between 2017 and 2025 was prioritized to align with the current periodontal classification and with recent consensus work. Searches of PubMed/MEDLINE, Scopus, and Web of Science combined terms related to periodontitis, systemic inflammation, C-reactive protein, interleukin-6, neutrophil-to-lymphocyte ratio, oxidative stress, genetic susceptibility, oral hygiene, ventilator-associated pneumonia, antimicrobial therapy, anti-inflammatory therapy, and exercise. Priority was given to consensus reports, clinical practice guidelines, systematic reviews and meta-analyses, randomized trials, and high-impact mechanistic reviews. Evidence was grouped according to the seven disciplinary domains specified for this review. Because no formal risk-of-bias scoring or quantitative pooling was performed, conclusions should be interpreted as an expert synthesis and not as pooled effect estimates. Readers should verify all citations against the original sources before formal publication.

3. Mechanistic Basis of the Oral–Systemic Inflammation Axis

3.1 Dysbiosis and host response

Modern models of periodontitis hold that disease is driven less by individual pathogens than by a dysbiotic shift in the entire subgingival community, which provokes a dysregulated, tissue-destructive host response (Figure 1). Keystone and accessory organisms subvert complement and neutrophil function, impairing microbial clearance while sustaining inflammation (Hajishengallis & Chavakis, 2021). The resulting inflammatory environment is rich in nutrients derived from tissue breakdown, which in turn favors further dysbiosis, creating a self-reinforcing cycle. Interleukin (IL)-1β, IL-6, tumor necrosis factor-alpha (TNF-α), IL-17, and prostaglandin E2 coordinate recruitment of neutrophils and monocytes and activate osteoclastogenic pathways that lead to alveolar bone loss. Current understanding supports host-modulation as a therapeutic concept, aiming to restore resolution of inflammation rather than simply suppress microbes (Hajishengallis et al., 2020).

3.2 Routes to systemic effects

Three overlapping routes are usually proposed. First, bacteremia arises from daily mastication, toothbrushing, and especially periodontal instrumentation, allowing oral organisms and their products, such as lipopolysaccharide, to reach distant tissues. Periodontal pathogens and their DNA have been detected in atheromatous plaques and other extra-oral sites (Bui et al., 2019). Second, inflamed periodontal tissue may release cytokines and acute-phase mediators into the circulation, stimulating hepatic production of C-reactive protein (CRP) and fibrinogen and promoting endothelial activation (Schenkein et al., 2020). Third, oral inflammation appears to prime the bone marrow and circulating myeloid cells, a phenomenon related to

trained innate immunity, so that neutrophils and monocytes become hyper-responsive even at sites remote from the mouth (Hajishengallis & Chavakis, 2021). Aspiration of oral secretions into the lower respiratory tract constitutes a fourth, anatomical route relevant to pneumonia in vulnerable patients.

3.3 Oxidative stress as a shared mediator

Activated neutrophils generate large quantities of reactive oxygen species (ROS) during the respiratory burst. In periodontitis, the balance between ROS production and antioxidant capacity is disrupted, damaging lipids, proteins, and DNA, amplifying NF-κB signaling, and contributing to connective tissue destruction. It has been argued that periodontitis is fundamentally an inflammatory disease of oxidative stress, a view with implications for both diagnosis and adjunctive therapy (Sczepanik et al., 2020). Systemically, oxidative modification of lipoproteins and endothelial dysfunction link the periodontal lesion with atherogenesis (Schenkein et al., 2020).

3.4 Bidirectionality and systemic modifiers

The axis operates in both directions. Uncontrolled diabetes, obesity, smoking, and certain hematological, immunological, and genetic conditions modify the course of periodontitis (Jepsen et al., 2018). Hyperglycemia, for example, increases advanced glycation end-product signaling and amplifies inflammatory cytokine production in the periodontium, while periodontal inflammation may worsen insulin resistance. Atherosclerosis itself is now understood as a chronic inflammatory disease in which innate immune pathways, including the NLRP3 inflammasome and IL-1β signaling, play causal roles (Libby, 2021). The convergence of these pathways with periodontal inflammation explains why measuring and reducing inflammatory burden is relevant across disciplines.

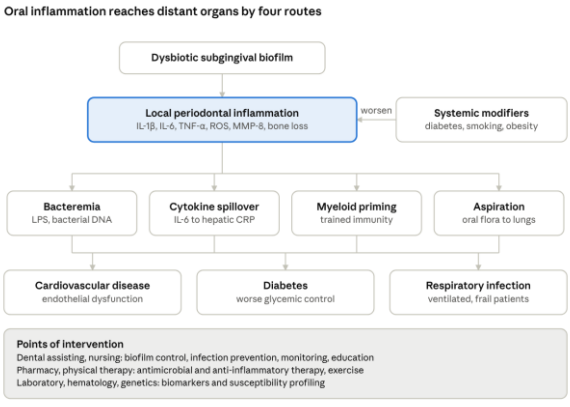


Figure 1. Conceptual model of the oral–systemic inflammation axis, showing dysbiotic biofilm, local periodontal inflammation, systemic transmission routes, and downstream systemic outcomes, with points of discipline-specific intervention.

4. Inflammatory Biomarkers, Cytokines, and Oxidative Stress

4.1 Acute-phase proteins and cytokines

Laboratory medicine provides the quantitative backbone of the oral–systemic model. High-sensitivity C-reactive protein (hs-CRP) is the most widely used marker of systemic low-grade inflammation, and its clinical relevance is supported by trials of anti-inflammatory therapy in cardiovascular disease, in which reductions in inflammation, independent of lipid lowering, were associated with fewer cardiovascular events (Ridker et al., 2017). Individuals with periodontitis show, on average, higher circulating CRP and IL-6, and periodontal therapy has been associated with short- to medium-term reductions in systemic inflammatory markers, although effects vary with disease severity, baseline inflammation, and treatment intensity (Herrera et al., 2023; Schenkein et al., 2020). In patients with type 2 diabetes, a randomized trial showed that intensive periodontal treatment improved glycemic control (HbA1c) at 12 months compared with community-based care, demonstrating that local inflammation control can produce measurable systemic metabolic benefit (D'Aiuto et al., 2018).

IL-6, IL-1β, and TNF-α provide mechanistic information but are less standardized for routine use because of assay variability, diurnal fluctuation, and short half-lives. In practice, hs-CRP, fibrinogen, and HbA1c are the most pragmatic circulating markers, interpreted alongside clinical periodontal parameters rather than in isolation.

4.2 Oral fluid biomarkers

Saliva and gingival crevicular fluid (GCF) are attractive noninvasive matrices. Systematic review evidence indicates that host-derived salivary biomarkers, notably matrix metalloproteinase-8 (MMP-8), IL-1β, and others, show moderate diagnostic accuracy for periodontitis, with sensitivity and specificity influenced by case definition, sampling procedure, and assay platform (Kc et al., 2020). Point-of-care MMP-8 assays offer chairside risk stratification, yet their role is adjunctive rather than replacing clinical probing and radiographic assessment.

4.3 Oxidative stress markers

Oxidative stress is assessed through markers of lipid peroxidation (malondialdehyde), oxidative DNA damage (8-hydroxy-2'-deoxyguanosine), total antioxidant capacity, and enzymatic antioxidants such as superoxide dismutase and glutathione peroxidase. Contemporary redox biology emphasizes that oxidative stress involves disruption of redox signaling and not solely accumulation of damaging oxidants, which complicates interpretation of single markers (Sies et al., 2017). In periodontitis, studies report elevated oxidants and depleted antioxidants in saliva, GCF, and serum, and levels partially normalize after periodontal therapy (Sczepanik et al.,

2020; Wang et al., 2017). Nevertheless, pre-analytical variables, lack of reference ranges, and inconsistent assays prevent routine clinical adoption.

4.4 Summary of biomarkers

Table 1 summarizes the principal laboratory and hematological markers relevant to the oral–systemic axis and highlights practical cautions.

Table 1. Principal laboratory and hematological markers of the oral–systemic inflammation axis

Domain	Marker	Biological meaning	Practical utility and cautions
Acute-phase proteins	hs-CRP	Hepatic response to IL-6; general low-grade inflammation	Widely available; informs cardiovascular inflammatory risk (Ridker et al., 2017); nonspecific and raised by infections, obesity, and smoking
Cytokines	IL-6, IL-1β, TNF-α	Drivers of acute-phase response, osteoclastogenesis, and endothelial activation	Mechanistically informative; limited standardization and high biological variability (Schenkein et al., 2020)
Oral fluid markers	Salivary/GCF MMP-8, IL-1β	Collagen degradation and local inflammatory activity	Noninvasive, chairside potential; moderate accuracy, adjunctive only (Kc et al., 2020)
Oxidative stress	MDA, 8-OHdG, total antioxidant capacity, SOD	Oxidant burden and antioxidant depletion	Research-oriented; lacks reference intervals (Sies et al., 2017; Wang et al., 2017)
Metabolic	HbA1c, fasting glucose	Glycemic control; modifier and outcome of periodontal inflammation	Essential in periodontal patients with diabetes (D'Aiuto et al., 2018)
Hematological	Neutrophil-to-lymphocyte ratio (NLR)	Balance of innate and adaptive immune activation	Inexpensive from routine blood count; influenced by steroids and stress (Zahorec, 2021)
Hematological	Total/differential leukocyte count, platelet indices	Cellular marker of inflammatory activation	Associations with periodontitis reported; effects modest (Botelho et al., 2021)

5. Inflammatory Blood Indices and Immune-Cell Alterations

5.1 Routine blood-count indices

The complete blood count is the most accessible window onto systemic immune status. Ratios derived from it, particularly the neutrophil-to-lymphocyte ratio (NLR), reflect the balance between innate neutrophil-driven inflammation and lymphocyte-mediated regulation. A review of the NLR concluded that it is a simple, inexpensive marker of systemic inflammatory stress, associated with outcomes across infection, cardiovascular disease, and malignancy, but also noted that interpretation requires attention to age, medications, and acute stressors (Zahorec, 2021). Population-based work in the Rotterdam Study established reference values for white-blood-cell-based inflammatory indices, including NLR, platelet-to-lymphocyte ratio, and systemic immune-inflammation index, and showed that these values vary with age, sex, and smoking, a reminder that context-specific reference intervals are required (Fest et al., 2018).

5.2 Periodontitis and circulating blood-cell profiles

A systematic review and meta-analysis found that individuals with periodontitis tend to display higher white blood cell and neutrophil counts, and in some analyses altered platelet and red-cell parameters, relative to periodontally healthy controls, supporting the notion that periodontal inflammation leaves a hematological signature (Botelho et al., 2021). Effect sizes were generally modest and heterogeneity was substantial, and confounders such as smoking, obesity, and diabetes were inconsistently controlled. The findings are most useful as hypothesis-supporting evidence for the systemic reach of periodontal inflammation, and not as a diagnostic tool. Hematological indices should therefore complement, not replace, periodontal examination.

5.3 Neutrophil, monocyte, and bone-marrow dynamics

Beyond static counts, the functional state of immune cells is central. Neutrophils in periodontitis can exhibit hyper-reactivity, excessive ROS generation, and dysregulated formation of extracellular traps, while circulating monocytes may adopt a primed, pro-inflammatory phenotype. These changes are consistent with inflammatory reprogramming of hematopoietic progenitors, a mechanism that could sustain systemic risk even after local inflammation subsides (Hajishengallis & Chavakis, 2021).

5.4 Clonal hematopoiesis and inflammation

An important emerging concept is clonal hematopoiesis of indeterminate potential (CHIP), in

which somatic mutations in genes such as *DNMT3A*, *TET2*, and *ASXL1* confer a competitive advantage on blood-cell clones. CHIP was associated with an increased risk of atherosclerotic cardiovascular disease in a landmark study (Jaiswal et al., 2017), and subsequent work indicates that mutant myeloid cells display enhanced inflammatory signaling, thereby linking aging, inflammation, and cardiovascular risk (Jaiswal & Ebert, 2019). Whether chronic periodontal inflammation interacts with clonal expansion remains a speculative but biologically attractive hypothesis, and one that illustrates how hematology can refine understanding of the axis.

5.5 Clinical interpretation

Hematologists and laboratory scientists can contribute by recommending standardized reporting of NLR and related indices, defining population-appropriate reference intervals, and advising on pre-analytical issues such as fasting status and time of day. For dental teams, unexplained marked leukocytosis, cytopenias, gingival bleeding disproportionate to plaque, or gingival enlargement should prompt medical referral because they may signal hematological disease rather than plaque-induced inflammation (Jepsen et al., 2018).

6. Susceptibility to Inflammatory Disorders

Individual variation in the response to the same plaque burden is striking, and a substantial part of it is heritable. Twin and family studies have long indicated moderate heritability for periodontitis, and modern genome-wide approaches are now defining specific loci. A review of the role of inflammation and genetics in periodontal disease emphasized that susceptibility reflects polygenic contributions that act predominantly through regulation of innate and adaptive immune responses, rather than through single high-penetrance mutations (Loos & Van Dyke, 2020). Rare severe forms with early onset, in contrast, may result from monogenic immune defects such as those affecting neutrophil number or function, which again highlights the central position of neutrophils in periodontal homeostasis.

A meta-analysis of genome-wide association studies of aggressive and chronic periodontitis identified novel risk loci and implicated genes involved in epithelial barrier function and immune regulation, supporting the idea that the genetic architecture overlaps with that of other inflammatory conditions (Munz et al., 2019). A subsequent large genome-wide analysis combining clinical and self-reported data for dental caries and periodontitis identified multiple loci, including those related to immune and inflammatory pathways, and illustrated both the promise and the heterogeneity of phenotyping in oral genetics (Shungin et al., 2019). Overlap between loci for periodontitis, cardiovascular disease, and diabetes, for example, within inflammatory pathways, has been proposed as a partial explanation for their frequent co-occurrence (Loos & Van Dyke, 2020).

From a translational standpoint, genetics offers three potential contributions. First, polygenic risk scores may eventually refine risk stratification and recall intervals, although current scores explain only a small fraction of variance and lack validated clinical thresholds. Second, genetic counseling and family history ascertainment can identify patients with early, severe disease who warrant medical evaluation for underlying immunodeficiency or syndromic conditions. Third, understanding shared genetic architecture may help in selecting targets for host-modulation therapy. At present, however, genetic testing for periodontitis susceptibility is not recommended for routine care, and ethical issues concerning privacy and over-interpretation must be addressed. Importantly, genetic susceptibility does not imply inevitability: environmental modifiers such as plaque control, smoking cessation, and glycemic management retain strong influence on outcomes.

7. Oral Hygiene, Periodontal Assessment, and Infection Prevention

7.1 Supporting mechanical biofilm control

Mechanical removal of the dental biofilm remains the foundation of both gingivitis management and periodontitis prevention, and it is the intervention most directly within the dental assistant's educational remit. A systematic review and meta-analysis found that poor oral hygiene is significantly associated with periodontitis, with the association strengthening as plaque accumulation increases (Lertpimonchai et al., 2017). Because patient behavior determines day-to-day plaque control, the repeated, individualized coaching that dental assistants deliver chairside is a clinically meaningful contribution and not an administrative one. Effective instruction addresses brushing technique, the choice of manual or powered brushes, and, critically, interdental cleaning, since toothbrushing alone does not reach approximal surfaces. A Cochrane review concluded that interdental brushes may reduce plaque and gingival inflammation more than toothbrushing alone, although the certainty of evidence varied by device and outcome (Worthington et al., 2019). A review of contemporary mechanical oral hygiene practices likewise emphasized that the choice of method and device should be individualized to the patient's anatomy, dexterity, and motivation (Sälzer et al., 2020).

Chemical adjuncts, such as chlorhexidine, cetylpyridinium chloride, and essential-oil rinses, can supplement mechanical control in patients with gingival inflammation, yet their benefit is adjunctive and accompanied by side effects such as staining and altered taste (Figuero et al., 2020). Dental assistants play a key role in explaining correct use, duration,

and the temporary nature of such adjuncts, thereby reinforcing rather than replacing mechanical hygiene.

7.2 Periodontal assessment and data capture

The staging and grading system depends on accurate collection of probing depth, clinical attachment level, bleeding on probing, recession, furcation involvement, tooth mobility, and radiographic bone loss (Tonetti et al., 2018). Where regulations allow, dental assistants contribute by preparing charts, recording dictated measurements, taking plaque and bleeding scores, exposing radiographs, and ensuring that systemic risk modifiers, including diabetes status, smoking, medications, and relevant laboratory values, are captured in the record. Scope of practice differs between jurisdictions, and diagnosis and treatment planning remain the responsibility of the dentist or periodontist. Nevertheless, structured data capture is essential to monitoring over time: bleeding-on-probing percentages and plaque scores are the clinical counterpart of laboratory inflammatory markers and allow trends to be tracked at each recall. Consensus definitions of periodontal health emphasize that stable health is characterized by minimal bleeding on probing and absence of inflammation, so these simple indices offer real clinical value (Chapple et al., 2018).

7.3 Infection prevention and control

Periodontal therapy generates aerosols and transient bacteremia, creating infection-control responsibilities that fall largely on the dental assistant. Core tasks include adherence to standard precautions, hand hygiene, appropriate personal protective equipment, instrument reprocessing and sterilization monitoring, surface disinfection, dental unit waterline management, sharps safety, and aerosol-mitigation measures such as high-volume evacuation. Medical history review before instrumentation helps identify patients at heightened risk from bacteremia, such as those with prosthetic cardiac valves or immunosuppression, so that the dentist can consider consultation with the patient's physician. In patients with severe periodontitis, the clinical practice guideline stresses a stepwise approach in which behavior change and supragingival biofilm control precede subgingival instrumentation, with reassessment of response before further steps (Sanz et al., 2020b). Dental assistants support each step by preparing the operatory and instruments, ensuring patient comfort, and reinforcing home-care instructions.

8. Systemic Inflammation Monitoring and Patient Education

8.1 Monitoring in vulnerable populations

Nurses are frequently the professionals who observe patients longest and most continuously, which positions them to detect and respond to oral and systemic inflammatory signals. The strongest evidence for nursing-delivered oral care comes from critical care. A Cochrane review of oral hygiene care for critically ill patients concluded that chlorhexidine mouthwash or gel probably reduces the incidence of ventilator-associated pneumonia, with no clear effect on mortality or duration of ventilation, and that evidence for toothbrushing is less certain (Zhao et al., 2020). These findings support systematic oral assessment, protocolized hygiene, and attention to secretion management in intubated, dysphagic, or institutionalized patients, in whom aspiration of oral flora is a plausible route for pulmonary infection (Herrera et al., 2023).

Beyond respiratory outcomes, nursing monitoring encompasses temperature, heart rate, respiratory rate, hydration, wound status, glycemic readings, and trends in laboratory markers such as CRP and leukocyte counts as reported by the laboratory. Rising or persistent elevations, unexplained fever, new oral pain, swelling, halitosis, or purulence should trigger escalation to the responsible clinician. Nurses in diabetes, cardiology, and oncology settings may also administer brief oral health screens, since glycemic control and periodontal inflammation interact bidirectionally and periodontal therapy can improve HbA1c (D'Aiuto et al., 2018).

8.2 Patient education and behavior change

Patient education is the second pillar of nursing contribution. Evidence-informed education emphasizes plain language, demonstration, and teach-back methods to confirm understanding. Key content includes twice-daily brushing with fluoride toothpaste, daily interdental cleaning, tobacco cessation, glycemic self-management, the warning signs of gum disease, and the importance of regular dental recall. Nurses can also explain that periodontal treatment is part of cardiometabolic risk management without overstating causal claims, consistent with consensus statements that the evidence supports association and biologic plausibility but not yet proof that periodontal therapy prevents cardiovascular events (Sanz et al., 2020a). Culturally sensitive education, attention to health literacy, and involvement of caregivers are particularly important in older adults, people with cognitive impairment, and those with limited access to dental care.

9. Anti-Inflammatory and Antimicrobial Medication Management

9.1 Antiseptics and antimicrobials

Pharmacists and prescribers face the challenge of balancing efficacy against adverse effects and antimicrobial resistance. Systemic antibiotics, usually amoxicillin with metronidazole, can provide modest additional improvements in probing depth and attachment when added to subgingival instrumentation in selected patients, but meta-analytic evidence also highlights heterogeneity, adverse events, and stewardship concerns (Teughels

et al., 2020). Locally delivered antimicrobials show limited and inconsistent additional benefit (Herrera et al., 2020). The European clinical practice guideline accordingly advises against routine use of adjunctive systemic antimicrobials and recommends reserving them for specific presentations, such as generalized severe periodontitis in young adults, after biofilm control has been optimized (Sanz et al., 2020b). Pharmacists support these decisions by verifying indications, dosing, interactions (for instance, metronidazole with alcohol or warfarin), allergy history, and renal and hepatic function, and by counseling patients on adherence and adverse effects.

Antiseptic mouthrinses are widely sold over the counter. Systematic review evidence supports adjunctive chlorhexidine, essential oils, and cetylpyridinium chloride for reducing plaque and gingivitis, with chlorhexidine producing the most pronounced effects but also staining and taste disturbance with prolonged use (Figuero et al., 2020). Pharmacists are well placed to advise on short-term versus long-term use and to identify patients for whom referral is more appropriate than self-medication.

9.2 Host modulation and systemic anti-inflammatory therapy

Because tissue damage in periodontitis is largely host-mediated, host-modulation strategies seek to restore resolution of inflammation. Sub-antimicrobial-dose doxycycline, which inhibits matrix metalloproteinases, is the best-established example, while experimental approaches target complement, IL-17, IL-1β, and specialized pro-resolving mediators (Hajishengallis et al., 2020). Such approaches are largely investigational for periodontitis.

In cardiovascular medicine, however, proof of concept for targeting inflammation exists. Canakinumab, an IL-1β monoclonal antibody, reduced recurrent cardiovascular events independent of lipid lowering in patients with prior myocardial infarction and elevated hs-CRP, though with an increase in fatal infections (Ridker et al., 2017). Low-dose colchicine (0.5 mg daily) reduced ischemic cardiovascular events after myocardial infarction (Tardif et al., 2019) and in chronic coronary disease (Nidorf et al., 2020), with signals for pneumonia and gastrointestinal effects that require monitoring. These trials were not designed to test periodontal outcomes, and no trial has yet shown that anti-inflammatory therapy for periodontitis lowers cardiovascular events. They nevertheless strengthen the rationale for treating inflammatory burden as a clinical target. Pharmacists contribute by medication reconciliation, screening for interactions (colchicine with strong CYP3A4 or P-glycoprotein inhibitors, for example), and monitoring for infection risk.

9.3 Medication-related oral considerations

Many drugs influence oral health. Anticholinergics, antidepressants, and antihypertensives can cause xerostomia, which increases plaque retention and caries risk; calcium channel blockers, phenytoin, and cyclosporine may cause gingival overgrowth that complicates plaque control; and long-term corticosteroids can alter immune responses and blood-count indices. Pharmacists can flag these effects, suggest saliva substitutes or formulation changes, and communicate with dental teams. Table 2 summarizes the main pharmacological strategies and the evidence base discussed above.

Table 2. Pharmacological strategies relevant to the oral–systemic inflammation axis

Strategy	Examples	Rationale	Evidence summary	Pharmacist considerations
Antiseptic mouthrinses	Chlorhexidine, cetylpyridinium chloride, essential oils	Reduce plaque and gingival inflammation; limit oral colonization	Adjunctive benefit for gingivitis (Figuero et al., 2020); lower ventilator-associated pneumonia incidence in ICU with chlorhexidine (Zhao et al., 2020)	Staining, taste change; limit duration; do not replace mechanical hygiene
Local antimicrobials	Chlorhexidine chips, minocycline microspheres, gels	Targeted subgingival antimicrobial delivery	Limited and inconsistent additional benefit (Herrera et al., 2020)	Reserve for residual localized pockets; cost and allergy review
Systemic antibiotics	Amoxicillin plus metronidazole	Suppress subgingival pathogens in selected severe cases	Modest additional improvement; adverse events and resistance concerns (Teughels et al., 2020; Sanz et al., 2020b)	Verify indication; screen for interactions and allergy; counsel on adherence
Host modulation	Sub-antimicrobial-dose doxycycline; experimental	Dampen destructive host response	Mechanistic rationale; largely investigational (Hajishengallis et al.,	Monitor use; avoid overlap with antimicrobial

	resolution-based agents		2020)	doses
Cytokine inhibition	Canakinumab (IL-1β)	Target innate inflammation in atherosclerosis	Fewer cardiovascular events; more fatal infections (Ridker et al., 2017)	Specialist setting; infection surveillance
Low-dose anti-inflammatory	Colchicine 0.5 mg daily	Inhibit inflammasome and neutrophil activity	Fewer ischemic events after MI and in chronic coronary disease (Tardif et al., 2019; Nidorf et al., 2020)	Check CYP3A4/P-gp interactions, renal function, GI effects

10. Exercise-Based Modulation of Systemic Inflammation

10.1 Mechanisms of exercise-induced immunomodulation

Physical inactivity is an established contributor to chronic low-grade inflammation, in part through accumulation of visceral adipose tissue that secretes pro-inflammatory adipokines (Furman et al., 2019). Regular exercise exerts the opposite effect through several overlapping mechanisms. Contracting skeletal muscle releases myokines, including IL-6, which in this context triggers anti-inflammatory signaling, increasing IL-10 and IL-1 receptor antagonist while dampening TNF-α production. A narrative review of exercise and cytokines described how acute bouts transiently raise circulating IL-6, whereas chronic training lowers basal pro-inflammatory tone and improves musculoskeletal and metabolic health (Docherty et al., 2022). Additional mechanisms include reduced visceral fat, improved insulin sensitivity, enhanced antioxidant defenses, and favorable shifts in immune-cell subsets and function. Importantly, the relationship between exercise dose and immunity is not linear: moderate, regular activity supports immune surveillance and lowers inflammation, while prolonged, exhaustive exertion without adequate recovery can induce transient immune suppression (Nieman & Wentz, 2019).

10.2 Clinical evidence

A systematic review and meta-analysis of randomized controlled trials in healthy middle-aged and older adults found that aerobic exercise training reduced circulating inflammatory markers, including CRP, IL-6, and TNF-α (Zheng et al., 2019). In people with metabolic disorders, a meta-analysis indicated that high-intensity interval training lowers some inflammatory markers, although results were heterogeneous across markers, populations, and protocols (Khalafi & Symonds, 2020). With regard to the oral cavity itself, a systematic review and meta-analysis reported that higher levels of physical activity were associated with a lower prevalence of periodontal disease (Ferreira et al., 2019). Most of the underlying studies are observational, and confounding by diet, smoking, body mass index, and socioeconomic status limits causal interpretation. Even so, the findings are coherent with the mechanistic literature and support exercise as a low-risk component of anti-inflammatory strategy.

10.3 Role of the physical therapist

Physical therapists translate this evidence into individualized prescriptions. Assessment includes cardiorespiratory fitness, strength, mobility, comorbidities, medications (for instance, beta-blockers or anticoagulants), and contraindications to exertion. Prescriptions typically combine aerobic training, resistance exercise, and balance or flexibility work, progressed gradually according to tolerance and organized by frequency, intensity, time, and type. For patients with cardiovascular disease, diabetes, chronic respiratory disease, or frailty, supervised rehabilitation programs offer safety monitoring and behavioral support. Therapists also educate patients on recovery, sleep, hydration, and nutrition, which influence inflammatory responses to training. Oral considerations include recommending protective mouthguards for contact activities, reminding patients to maintain hygiene routines, and noting that dry mouth from mouth breathing and sports drinks can raise caries and erosion risk. Collaboration with dental and medical teams is advisable when surgical or intensive periodontal procedures are scheduled, so exercise timing can be adapted (Figure 2).

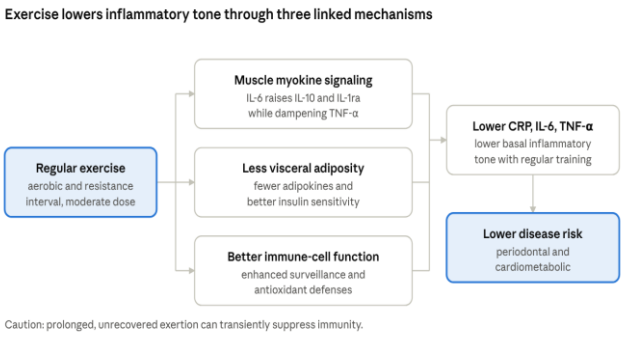


Figure 2. Proposed pathways through which regular exercise modulates systemic inflammation, linking skeletal-muscle myokine signaling, reduced visceral adiposity, and improved immune-cell function with downstream effects on circulating markers and periodontal and cardiometabolic risk.

11. An Integrated Interprofessional Framework

11.1 Integrating the seven domains

The preceding sections show that each discipline controls a different node of the same network. The laboratory and hematology quantify inflammatory burden and its cellular correlates. Medical genetics explains part of the variability in individual responses. Dental assisting and nursing deliver the daily preventive, monitoring, and educational activities that reduce microbial and inflammatory load. Pharmacy ensures that antimicrobial and anti-inflammatory agents are used safely and where evidence supports them. Physical therapy addresses the systemic and behavioral side of the equation by modulating inflammation through exercise. Because no single profession can influence all of these nodes, effective care requires shared goals and structured communication.

We propose a four-stage pathway, illustrated in Figure 3. In the first stage, screening and risk identification, the dental team collects periodontal data and systemic history, the nurse records vital signs and comorbidities, and the laboratory supplies baseline markers such as hs-CRP, HbA1c, and a complete blood count with derived indices. Genetic counseling is triggered by early-onset severe disease or relevant family history. In the second stage, intervention, biofilm control and non-surgical periodontal therapy are provided, medications are reconciled and optimized by the pharmacist, and the physical therapist initiates an exercise program. In the third stage, monitoring, bleeding on probing and plaque scores are tracked alongside inflammatory markers, and nursing observations identify deterioration or complications. In the fourth stage, maintenance and escalation, patients enter supportive periodontal care with individualized recall intervals, and persistent inflammation despite adequate periodontal therapy prompts medical evaluation for hematological, metabolic, or immunological causes.

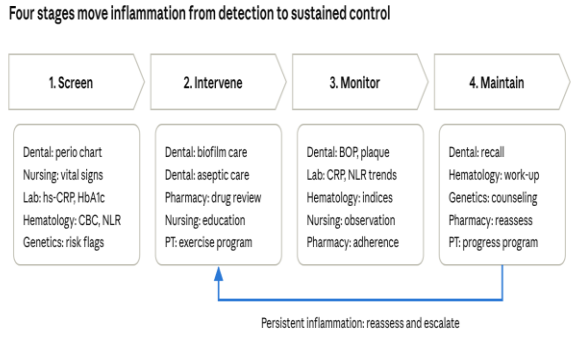


Figure 3. Proposed four-stage interprofessional pathway for managing the oral–systemic inflammation axis, showing the contributions of the seven disciplines at each stage and the feedback loop from monitoring to escalation.

11.2 Practical principles

Several principles can support implementation. First, a minimal shared dataset should be defined, comprising periodontal stage and grade, bleeding on probing, hs-CRP, HbA1c, a blood-count profile, smoking status, current medications, and physical-activity level. Second, referral thresholds and communication channels should be agreed between dental, medical, and laboratory services so that findings such as marked leukocytosis or persistently elevated CRP are acted on. Third, patient messaging should be consistent across professions, framing oral care as part of general health while respecting the present limits of causal evidence (Herrera et al., 2023). Fourth, scopes of practice should be respected, with each profession contributing within its competence and legal framework. Finally, the model should be person-centered, accounting for patient preferences, access barriers, and health literacy.

12. Limitations and Research Priorities

This review has several limitations. As a narrative synthesis, it is vulnerable to selection bias and lacks formal quality appraisal. The evidence base is uneven: periodontal medicine, laboratory biomarkers, and cardiometabolic pharmacology are well represented, while evidence on dental assistant-specific interventions, nursing protocols outside intensive care, and exercise interventions explicitly targeting periodontal outcomes is thin. Much of the association evidence is observational and vulnerable to residual confounding by smoking, obesity, diabetes, and socioeconomic status. Biomarker studies suffer from assay heterogeneity and the absence of standardized reference ranges. The framework proposed here is conceptual and has not been empirically validated.

Future research should prioritize several directions. Pragmatic randomized trials are needed to test whether periodontal therapy combined with structured exercise or pharmacological optimization yields greater reductions in systemic inflammation and cardiometabolic events than either alone. Standardized biomarker panels, combining hs-CRP, blood-count indices, and validated salivary markers, should be developed and validated against clinical outcomes. Genetic risk stratification requires prospective evaluation of clinical utility and ethical implications. Studies should examine the contribution of clonal hematopoiesis and trained innate immunity to periodontal and systemic inflammation. Implementation research is needed to evaluate interprofessional pathways, task-sharing models, and cost-effectiveness across health systems, including low-resource settings.

13. Conclusion

The oral–systemic inflammation axis provides a coherent scientific rationale for integrating

oral health into general health care. Periodontal inflammation contributes to systemic inflammatory burden through bacteremia, cytokine spillover, oxidative stress, and immune-cell priming, while systemic conditions in turn shape periodontal outcomes. Laboratory and hematological markers offer practical tools for monitoring, genetics clarifies susceptibility, and dental assisting, nursing, pharmacy, and physical therapy each provide evidence-based means of reducing inflammatory load. Although causal evidence that periodontal care improves hard systemic outcomes remains incomplete, the consistency of mechanistic and clinical findings supports coordinated, preventive, interprofessional care. Adopting shared datasets, clear referral pathways, and unified patient messaging is a feasible next step toward realizing this model in practice.

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