



## **Cal-Systemic Health and Disorders: Latest Prospects on Oral Antisepsis**

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A growing body of evidence supports the inter-connections between oral dysbiosis [1–4] and systemic infections [5], as well as inflammatory [6–8], degenerative [9], and neoplastic diseases [10,11].

In detail, in subjects with periodontitis and peri-implantitis, bacterial-associated destructive inflammatory diseases of the tissue supporting the teeth [12,13] and surrounding dental implants [14,15], microorganisms from inflamed tissues may gain access to the systemic circulation and reach distant organs. Alternatively, periodontal pathogens may directly increase sera levels of bacterial virulence factors and indirectly of pro-inflammatory cytokines, consequently, inducing so-called systemic inflammation [16]. Moreover, it is well-known that in subjects with acute odontogenic infections and mainly dental abscesses, pyogenic bacteria can eventually spread, leading to systemic involvement and sepsis syndrome [17]. Furthermore, it has been proposed that oral and periodontal microorganisms may translocate to the gastrointestinal and respiratory tracts through microaspiration by contiguity, also in physiological conditions [18]. In this regard, emerging findings associate pulmonary and systemic infections with the oral and periodontal microbiome [19].

Indeed, considerable evidence suggests that, in the absence of effective oral care, gingival biofilm composition undergoes quantitative and qualitative modifications, mainly hosting Gram-negative pathogens, which may be passively transported to the upper and lower airways, and, subsequently, determine lung infections [1,19]. This pathogenic mechanism may be especially relevant in patients requiring elective intubation and mechanical ventilation and in those admitted to intensive care units, who may be more prone to ventilator-associated pneumonia [20]. Thus, it may be hypothesized that subjects undergoing prolonged mechanical ventilation may be, due to their compromised general conditions, even more susceptible to oral, lung, and, secondarily, gut dysbiosis, further enhancing the risk of infection.

Such a consideration may be crucial for healthcare-associated infections (HAIs), especially those caused by multidrug-resistant (MDR) bacteria, which are associated with prolonged length of hospitalization and increased morbidity, mortality, and healthcare costs [21]. In addition, since surgical procedures are increasingly performed on older patients with more comorbidities, it is expected that the incidence of HAIs will further increase unless prevention is improved [21,22].

Colonizing the host by potentially pathogenic microorganisms is a prerequisite for developing HAIs. Although potentially pathogenic microorganisms can be transmitted to patients from the hands of healthcare workers and contaminated equipment and fomites, the patient's microbiota is considered the primary source [5]. Consequently, considerable efforts have been made to reduce the occurrence of HAIs in peri-operative settings, especially in patients undergoing elective surgery [23]. The main goal of HAI preventive strategies relies on eradicating potentially pathogenic microorganisms from the skin, oropharynx, stomach, and gut, through antimicrobial therapy and antisepsis.

However, in order to preserve the recommended antimicrobial stewardship measures, the overuse and misuse of antibiotics should be avoided. Such an inappropriate antibiotic administration, coupled with poor patient adherence to antimicrobial therapy [24], indeed,



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**Copyright:** © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). plays an essential role in increasing bacterial resistance [22], which, in turn, leads to an increased risk of treatment failure, complications, and mortality, consequent to infections. Raising awareness about antimicrobial resistance, which constitutes, to date, a global publichealth problem, also increasing healthcare costs, has driven the field toward short-term antimicrobial treatments and appropriate antibiotic prescriptions. Coherently, the HAI preventive strategies have been progressively focused on antisepsis, which may positively affect the skin, oral, gut, and lung microbiome and, in turn, prevent dysbiosis and related disorders and minimize systemic infections.

Despite these considerations, oral decontamination or prophylaxis with oral antiseptics is not currently part of the standard routine care during hospitalization. Indeed, available Evidence-based Enhanced Recovery After Surgery (ERAS) protocols [23], aiming to minimize the length of hospital stay, HAIs, and readmissions, and optimize patient experience, do not currently include oral antisepsis. Conversely, several skin antisepsis protocols are routinely applied and have been found effective in preventing HAIs and surgical-site infections [21]. With the same aims, oral antisepsis protocols have been proposed in the last few decades to prevent the development of HAIs, especially in intensive care settings [21,25,26]. Following major elective surgery, a significant reduction in postoperative HAIs and pneumonia has been reported in subjects who underwent peri-operative oral antisepsis with chlorhexidine used as a mouthwash [21]. Povidone-iodine [27] and polyhexanide [28] mouth rinses may also be proven to be an effective alternative to chlorhexidine, especially in preventing MDR infections. In this context, peri-operative gingival biofilm control and oral hygiene may also be beneficial [29].

In addition to that, since periodontal pockets are considered a potential reservoir of bacteria and viruses [30], oral and periodontal infection control may be regarded as an adjunctive strategy to reduce the risk of HAIs and MDR infections. In this perspective, periodontal treatment, including the mechanical removal of supragingival and subgingival biofilm and calculus, may be indicated in the preoperative management of subjects undergoing elective surgery and requiring intubation. Preoperative periodontal debridement may be particularly appropriate in periodontal subjects, decreasing the risk of systemic dissemination of bacterial cells and virulence factors and pro-inflammatory mediators [31]. Additionally, preoperative biofilm control and periodontal health maintenance may be even more relevant in subjects with comorbidities. Indeed, those suffering from non-communicable diseases often show worse oral and periodontal conditions and, secondary to the proposed associations between oral and systemic health and disorders, altered immune–inflammatory response also against pathogens. This evidence supports, once again, the need for integrated preventive strategies for a comprehensive oral and general healthcare [32], combining population-based and individualized surveillance approaches.

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