



# The oral exposome – integrating environmental determinants into the etiology of oral pathologies

Ekspozom jamy ustnej: uwarunkowania środowiskowe w etiologii schorzeń jamy ustnej

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Krzyżanowska M, Drużdżel A, Parfienowicz Z, Curzytek K, Szczupaj M. The oral exposome – integrating environmental determinants into the etiology of oral pathologies. *Med Srodow.* doi:10.26444/ms/220058

## Abstract

**Introduction.** Oral diseases remain a major global health challenge, affecting app. 3.5 billion people. While traditional etiological models have focused primarily on behavioural and microbial factors, the disproportionate disease burden in industrializing regions suggests the presence of overlooked non-behavioural determinants.

**Objective.** The aim of the review is to synthesize current literature regarding the ‘oral exposome’ analyzing how environmental determinants—specifically atmospheric pollutants, heavy metals and chemical contaminants impact oral health throughout the lifespan.

**Brief description of the state of knowledge.** Recent research suggests that environmental toxicants may act as systemic stressors, potentially compromising oral homeostasis through a variety of mechanisms. Regarding dental caries, exposure to second-hand smoke (SHS) suppresses local immune responses, while heavy metals, such as lead, induce enamel hypoplasia via ionic substitution in the hydroxyapatite lattice. Periodontal health is similarly modulated by environmental factors, fine particulate matter and cadmium exposure trigger systemic oxidative stress and inflammation, accelerating alveolar bone resorption. Furthermore, maternal exposure to ambient air pollution and occupational hazards acts as a critical teratogen for orofacial clefts, particularly when interacting with genetic variants in folate metabolism. Finally, longitudinal data implicate gaseous pollutants and formaldehyde in the pathogenesis of nasopharyngeal carcinoma.

**Summary.** Evidence necessitates integrating environmental risk assessment into preventive dentistry. Pollutants are involuntary risk factors acting synergistically with other determinants. Mitigation strategies are urgent for reducing the disease burden and informing policy.

## Key words

tobacco smoke pollution, exposome, oral health, environmental pollutants

## Streszczenie

**Wprowadzenie i cel pracy.** Choroby jamy ustnej pozostają istotnym globalnym wyzwaniem zdrowotnym, dotycząc około 3,5 mld ludzi. Gdy tradycyjne modele etiologiczne skupiały się głównie na czynnikach behawioralnych i mikrobiologicznych, nieproporcjonalne obciążenie chorobami w regionach uprzemysłowujących się sugeruje obecność przeoczonych determinantów niebehawioralnych. Niniejszy przegląd ma na celu syntezę obecnej literatury na temat ekspozomu jamy ustnej, a także przedstawienie analizy, w jaki sposób determinanty środowiskowe (zanieczyszczenia atmosferyczne, metale ciężkie i zanieczyszczenia chemiczne) wpływają na zdrowie jamy ustnej w ciągu życia.

**Opis stanu wiedzy.** Badania sugerują, że toksyny środowiskowe działają jak stresory, zaburzając homeostazę jamy ustnej. W próchnicy narażenie na bierne palenie (SHS) osłabia odporność, a metale ciężkie (np. ołów) wywołują hipoplazję szkliwa poprzez substytucję jonową. Drobnny pył i kadm wpływają na przyzębie, wywołując stres oksydacyjny i zapalenie, co przyspiesza resorpcję kości. Ponadto narażenie kobiety w ciąży na zanieczyszczenie powietrza atmosferycznego i zagrożenia zawodowe działa jako krytyczny teratogen powodujący rozszczepy ustno-twarzowe płodu. Badania wiążą też zanieczyszczenia gazowe i formaldehyd z rakiem nosogardła.

**Podsumowanie.** Dowody wskazują na konieczność włączenia oceny ryzyka środowiskowego do profilaktyki stomatologicznej. Zanieczyszczenia są mimowolnymi czynnikami ryzyka działającymi synergistycznie z innymi determinantami. W celu zmniejszenia obciążenia chorobami i kształtowania polityki zdrowotnej niezbędne są strategie łagodzące skutki tych zjawisk.

## Słowa kluczowe

zdrowie jamy ustnej, zanieczyszczenie dymem tytoniowym, zanieczyszczenia środowiskowe, ekspozom

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## INTRODUCTION

Oral diseases remain among the most prevalent non-communicable diseases (NCDs) globally, affecting an estimated 3.5 billion people worldwide, according to the most recent assessment by the World Health Organization's [1]. Traditionally, the etiological models of major oral pathologies – specifically dental caries, periodontal disease, and oral malignancies – have been viewed primarily through the lens of behavioural and microbial factors. The 'ecological plaque hypothesis' and the role of fermentable carbohydrates have long dominated the discourse on caries, while poor oral hygiene and tobacco use have been cited as the primary drivers of periodontal degradation and oral cancers [2]. However, despite significant advancements in hygiene education and localized preventive measures, the burden of oral disease remains disproportionately high in rapidly industrializing regions, suggesting the existence of overlooked, non-behavioural determinants. Epidemiological data underscore this disparity, revealing that while the global prevalence of untreated dental caries in permanent teeth is approximately 29%, certain industrialized and urbanizing regions in East Asia and South-East Asia report significantly higher age-standardized prevalence rates compared to lower-income, less industrialized regions in Sub-Saharan Africa [1, 2]. Furthermore, research indicates that the transition from traditional to industrialized environments is associated with a 15–20% increase in the incidence of periodontal diseases, a trend particularly evident in urban centers where environmental pollution levels are highest [2, 3]. For instance, the incidence of oral and nasopharyngeal malignancies is nearly three times higher in industrialized areas of South-East Asia (9.1 per 100,000) compared to many African nations (under 3.0 per 100,000), where industrial atmospheric emissions are less concentrated [1, 4].

Contemporary epidemiological evidence necessitates a paradigm shift towards the concept of the 'oral exposome' – the cumulative measure of environmental influences and associated biological responses throughout the lifespan [5]. As the primary portal of entry for respiration and ingestion, the oral cavity is uniquely susceptible to environmental toxicants. Recent studies have indicated that environmental pollutants, including ambient air pollution (particulate matter), heavy metals and endocrine-disrupting chemicals, act as systemic stressors that compromise oral homeostasis [3].

The mechanisms linking environmental pollution to oral health are increasingly understood to be pluripotential. Inhalation of fine particulate matter ( $PM_{2.5}$ ) and nitrogen dioxide ( $NO_2$ ) has been shown to induce systemic oxidative stress and inflammation, pathways that are intrinsically linked to the pathogenesis of periodontitis and the disruption of host immune defenses [6]. Furthermore, exposure to heavy metals such as lead (*Pb*) and cadmium (*Cd*) – whether through atmospheric emission or contaminated water – has been implicated in the disruption of amelogenesis and the structural integrity of mineralized tissues, thereby increasing susceptibility to caries independent of dietary sugar intake [7].

Moreover, the teratogenic potential of environmental hazards poses a critical risk during embryogenesis. The intersection of maternal exposure to pollutants and genetic susceptibility has been identified as a significant cofactor in the etiology of orofacial clefts, challenging the view that these anomalies are purely genetic or idiopathic [8].

The aim of the review is to synthesize the current body of literature regarding the impact of environmental determinants on oral health. By examining the roles of second-hand smoke, atmospheric particulate matter, heavy metals, and chemical contaminants, the review highlights the urgent need to integrate environmental mitigation strategies into the framework of preventive dentistry and public health policy.

## OBJECTIVE

The primary objective of this review is to synthesize contemporary literature regarding the 'oral exposome' – defined as the cumulative measure of environmental influences and associated biological responses throughout the human lifespan. Specifically, the article aims to analyze how environmental determinants, including atmospheric pollutants, heavy metals, and chemical contaminants, act as systemic stressors that compromise oral homeostasis. Furthermore, the review seeks to highlight the necessity of integrating environmental risk assessment and mitigation strategies into the existing framework of preventive dentistry and public health policy to address the global burden of oral disease.

In order to identify relevant literature on the impact of environmental factors on oral health, a comprehensive search was conducted in electronic databases, including PubMed, Scopus, Web of Science and the World Health Organization (WHO) library. The search strategy focused on peer-reviewed articles, systematic reviews, and meta-analyses published mainly in the last 10 years to include current epidemiological data.

## MATERIALS AND METHOD

**Search Strategy.** To identify relevant literature regarding the impact of environmental determinants on oral health, a comprehensive search was conducted in major electronic databases, including PubMed, Scopus, Web of Science, and the World Health Organization (WHO) library. The search strategy focused on articles published primarily in the last decade to ensure the inclusion of contemporary epidemiological data.

The search utilized Boolean operators combining Medical Subject Headings (MeSH) and free-text terms related to oral outcomes and environmental exposures. Key words included combinations of: 'oral health', 'dental caries', 'periodontal disease', 'orofacial clefts', 'head and neck cancer', with 'air pollution', 'particulate matter' ( $PM_{2.5}$ ,  $PM_{10}$ ), 'heavy metals' (lead, cadmium), 'environmental tobacco smoke', 'endocrine disrupting chemicals' (BPA, phthalates), and 'exposome'.

The review prioritized high-level evidence, specifically including systematic reviews, meta-analyses, and large-scale cross-sectional studies (e.g., NHANES data). Inclusion criteria were defined as: (1) peer-reviewed studies published in English; (2) studies investigating the association between non-behavioural environmental factors and oral pathologies in human populations, and (3) toxicological studies elucidating biological mechanisms (e.g., oxidative stress, endocrine disruption), where relevant. Case reports, editorials, and studies focusing solely on genetic factors without an environmental component were excluded.

**Environmental determinants of dental caries.** While the etiology of dental caries is fundamentally driven by the interaction between fermentable carbohydrates and cariogenic bacteria, contemporary epidemiological evidence necessitates a broader consideration of environmental determinants. Beyond behavioural factors, exposure to environmental toxicants – specifically environmental tobacco smoke (ETS), atmospheric particulate matter (PM), and heavy metals – has emerged as a significant modulator of caries susceptibility.

Recent meta-analyses have indicated a robust positive correlation between exposure to second-hand smoke (SHS) and the prevalence of dental caries, particularly in the primary dentition of children. Systematic reviews indicate that children exposed to SHS demonstrate significantly higher salivary cotinine levels, which correlates with an altered oral microbiome and reduced salivary buffering capacity [9]. The mechanism appears to be two-fold: ETS exposure not only facilitates the colonization of cariogenic pathogens, but also suppresses the local immune response, thereby increasing the risk of early childhood caries. Furthermore, limited evidence suggests that maternal smoking during pregnancy may disrupt amelogenesis, leading to enamel hypoplasia, a known predisposing factor for carious lesions [10].

It is also noteworthy that recent toxicological assessments have highlighted the impact of heavy metals, specifically lead (Pb) and cadmium (Cd), on hard tissue mineralization. Environmental exposure to lead, even at low blood concentrations, has been associated with a higher prevalence of caries. The biological plausibility of this association rests on the capacity of  $Pb^{2+}$  ions to substitute for  $Ca^{2+}$  ions in the hydroxyapatite crystal lattice during tooth formation. This ionic substitution results in enamel with increased solubility and reduced stability against acidic challenges [11]. Similarly, co-exposure to cadmium has been linked to distinct alterations in salivary gland function and enamel porosity. Cross-sectional studies utilizing NHANES data have consistently reinforced the hypothesis that environmental burden of these nephrotoxic and osteotoxic metals contributes to poor oral health outcomes, independent of socio-demographic confounders [7].

Moreover, the scope of environmental cariology has recently expanded to include endocrine-disrupting chemicals (EDCs), particularly bisphenols and phthalates. Systematic reviews demonstrate a significant association between exposure to bisphenol A (BPA) and caries prevalence, attributed to the disruption of ameloblast activity and enamel matrix protein expression [12]. These ubiquitous compounds appear to induce Molar Incisor Hypomineralization (MIH), creating porous enamel defects that are rapidly colonized by cariogenic biofilm, thus accelerating lesion progression independent of dietary sugars [13].

Concurrently, emerging research suggests a potential link between ambient air pollution—specifically particulate matter with a diameter of less than 2.5 micrometers ( $PM_{2.5}$ ) and 10 micrometers ( $PM_{10}$ ) and oral health pathologies. Although the direct mechanism remains under investigation, it is postulated that chronic exposure to high levels of PM induces systemic inflammation and oxidative stress, which may impair the host defence mechanisms within the oral cavity. Moreover, poor air quality is frequently associated with increased mouth breathing due to nasal congestion; this habit causes xerostomia (dry mouth), thereby eliminating

the protective, washing effect of saliva and fostering an acidic environment conducive to demineralization [14]. Consequently, these findings suggest that environmental mitigation strategies should be considered an integral component of preventive dentistry.

#### **Impact of environmental pollutants on periodontal health.**

Environmental factors have increasingly been recognized as significant determinants of periodontal health, extending beyond the traditional scope of microbial etiology. Foremost among these is Second-hand Smoke (SHS), which has been consistently associated with the deterioration of periodontal parameters. Epidemiological evidence indicates a positive correlation between exposure to environmental tobacco smoke and adverse periodontal outcomes, specifically affecting the Gingival Index (GI), Clinical Attachment Loss (CAL), and Pocket Depth (PD). A systematic review and meta-analysis conducted by Shao et al. (2023) demonstrated that individuals exposed to SHS exhibit a significantly higher prevalence of moderate to severe periodontitis compared to non-exposed individuals, with cotinine levels serving as a biological marker directly proportional to the severity of attachment loss and tooth loss [15]. The biological plausibility of this association lies in the capability of SHS to impair gingival microcirculation and suppress the host immune response, thereby facilitating microbial invasion and tissue destruction.

In light of the mechanisms associated with tobacco combustion, it is crucial to address the emerging prevalence of electronic cigarettes (e-cigarettes). While often marketed as a safer alternative, recent investigations suggest that e-cigarette aerosol induces oxidative stress and inflammatory cytokine release in periodontal ligament fibroblasts, similar to conventional cigarettes. Studies indicate that the thermal degradation of humectants in e-liquids generates reactive aldehydes, which may contribute to increased gingival inflammation and altered repair mechanisms, even in the absence of combustion-derived tar [16].

Furthermore, the scope of environmental risk factors extends to ambient air pollution, particularly Particulate Matter (PM). Fine particulate matter  $PM_{2.5}$  has been identified as a systemic inflammatory agent that may exacerbate periodontal inflammation. Research analyzing the association between long-term exposure to  $PM_{2.5}$  and periodontal health suggests that inhaled particles can translocate into the systemic circulation, triggering a cascade of oxidative stress and systemic inflammation that compromises alveolar bone integrity [17]. This correlation highlights the role of respiratory pollutants as modifiable risk factors for periodontal degeneration.

Parallel to airborne pollutants, exposure to heavy metals and endocrine-disrupting chemicals presents a significant, albeit less visible, threat to the periodontium. Lead (Pb) and Cadmium (Cd) are of particular concern due to their ability to accumulate in calcified tissues. Data from the National Health and Nutrition Examination Survey (NHANES) has revealed that elevated blood cadmium levels are significantly associated with periodontitis, likely due to cadmium's osteotoxic properties which disrupt calcium metabolism and accelerate alveolar bone resorption [18]. Similarly, environmental exposure to phthalates—ubiquitous plasticizers found in consumer products—has been linked to oxidative stress and insulin resistance, pathways that

intersect with the pathogenesis of periodontal disease. Recent toxicological assessments suggest that phthalate exposure may potentiate gingival inflammation, modifying the host response to periodontal pathogens [19].

### **Environmental pollution and orofacial clefts (OFCs).**

Maternal exposure to second-hand smoke (SHS) constitutes a significant, yet preventable, environmental risk factor for orofacial clefts (OFCs). While active maternal smoking is a well-established teratogen, recent meta-analyses indicate that passive exposure carries a comparable risk profile, particularly due to the inability of the developing foetus to detoxify tobacco-derived carcinogens [20]. In the light of recent molecular findings, this correlation appears to be mediated through complex gene-environment interactions rather than direct toxicity alone. Specifically, SHS has been observed to modulate the expression of critical developmental genes. Epigenetic studies suggest that components of tobacco smoke may alter the methylation patterns of genes such as *RUNX2* and *IRF6*, which are pivotal for craniofacial bone formation and epithelial fusion [21]. Furthermore, perturbations in the signalling pathways involving *BMP4* and *SPRY2* have been identified in response to hypoxia and oxidative stress induced by smoke exposure, thereby disrupting the delicate regulatory network required for lip and palate closure [22].

Expanding the scope of environmental risk from the domestic to the ambient sphere, air pollution represents a pervasive hazard. The correlation between ambient air pollutants -specifically fine particulate matter ( $PM_{2.5}$ ), nitrogen dioxide ( $NO_2$ ) and sulfur dioxide ( $SO_2$ ) and the incidence of OFCs – is statistically significant, particularly when exposure occurs during the critical window of organogenesis [8]. This period, corresponding to the second month of gestation (weeks 5–9), coincides with the peak phases of palatogenesis. It is postulated that ultrafine particles and gaseous pollutants penetrate the placental barrier, inducing systemic oxidative stress and inflammation in fetal tissues [23]. This biological plausibility is supported by data indicating that maternal exposure to high concentrations of  $PM_{2.5}$  during this specific gestational window impedes cellular migration and proliferation in the developing maxilla, acting via mechanisms distinct from, yet additive to, those of tobacco smoke [24].

In addition to ubiquitous ambient pollutants, occupational exposure to specific chemical agents remains a critical determinant of OFC risk. Recent epidemiological investigations have highlighted a robust association between maternal occupational exposure to pesticides and organic solvents and an increased prevalence of cleft lip, with or without cleft palate [25]. These agents, often encountered in agricultural and industrial settings, act as endocrine disruptors and teratogens. A systematic review of occupational hazards indicates that the risk is particularly elevated for mothers handling glycol ethers and aliphatic aldehydes without adequate protective equipment during the first trimester [26]. Consequently, the etiology of OFCs must be viewed as multifactorial, where the cumulative burden of passive smoke, ambient pollution, and occupational chemical exposure interacts with genetic susceptibility to compromise craniofacial development.

Beyond atmospheric pollutants and organic solvents, maternal exposure to heavy metals—specifically cadmium

(Cd), lead (Pb), and arsenic (As)—constitutes a critical area of investigation regarding OFC etiology. Heavy metals act as potent teratogens capable of crossing the placental barrier and accumulating in fetal tissues. Recent toxicological assessments suggest that cadmium exposure, often stemming from industrial emissions or contaminated food sources, interferes with calcium signalling pathways and zinc homeostasis, both of which are essential for neural crest cell migration [27]. A recent meta-analysis confirms a positive correlation between maternal blood cadmium levels and the risk of cleft lip and palate, suggesting that cadmium-induced oxidative stress may trigger apoptosis in the developing palatal shelves [28]. Furthermore, co-exposure to lead has been shown to exacerbate these effects, indicating a synergistic toxicity that disproportionately affects embryonic development during the first trimester.

Concurrently, environmental risk assessment must extend to hydrological reservoirs, specifically focusing on water contaminants. Disinfection by-products (DBPs), such as trihalomethanes (THMs), which form when chlorine reacts with organic matter in water systems, have emerged as potential risk factors. Epidemiological evidence indicates that maternal consumption of water containing high concentrations of total THMs is associated with a modest but statistically significant increase in the risk of birth defects, including OFCs [29]. The biological mechanism is hypothesized to involve the interference of DBPs with folate metabolism. Since folate is a critical cofactor in DNA synthesis and methylation, its disruption by waterborne contaminants can mimic the effects of dietary folate deficiency, thereby increasing susceptibility to craniofacial anomalies [30].

It is imperative to note that environmental pollutants do not act in isolation; their teratogenic potential is frequently modulated by maternal and foetal genetic architecture. This interaction is most evident in the folate metabolic pathway. Variants in the *MTHFR* (methylentetrahydrofolate reductase) gene, particularly the C677T polymorphism, have been extensively studied as susceptibility factors. Recent literature suggests that the adverse effects of air pollution ( $PM_{2.5}$  and  $NO_2$ ) and cigarette smoke are significantly amplified in mothers carrying the risk alleles for *MTHFR* [31]. These findings support the hypothesis that environmental pollutants may deplete systemic folate levels or inhibit key enzymes in the one-carbon metabolism cycle. Consequently, in genetically susceptible individuals, even low-level exposure to environmental toxicants may lower the threshold for OFC occurrence by disrupting the methylation of DNA required for the precise regulation of craniofacial development genes [32].

While tobacco consumption and alcohol abuse have historically been recognized as the primary carcinogenic drivers for Head and Neck Cancers (HNC), contemporary epidemiological data necessitates a broader investigation into environmental co-factors. In the light of recent findings, there is accumulating evidence that long-term exposure to ambient air pollution and specific occupational hazards plays a significant, yet underappreciated, role in the pathogenesis of malignancies such as Nasopharyngeal Carcinoma (NPC) and oral cavity cancers. Unlike lifestyle factors, which are often these environmental determinants represent involuntary risks that disproportionately affect populations in rapidly industrializing regions.

Specifically, the inhalation of fine particulate matter

**Table 1.** Mechanistic pathways and target tissues of environmental pollutants contributing to dental caries susceptibility

Environmental Agent	Primary Pathophysiological Mechanism	Critical Exposure Window	Distinctive Oral Sequelae (Beyond Caries)	Source
Environmental Tobacco Smoke (ETS)	Salivary Modification: Reduction in salivary buffering capacity and suppression of salivary immunoglobulin A (IgA), facilitating cariogenic bacterial overgrowth.	Early Childhood (Primary Dentition)	Gingival pigmentation; delayed tooth eruption; altered oral microbiome diversity.	[9, 10]
Lead (Pb)	Ionic Substitution: Incorporation of Pb <sup>2+</sup> into the hydroxyapatite crystal lattice in place of Ca <sup>2+</sup> , resulting in structural instability and increased acid solubility.	Pre-natal ( <i>in utero</i> ) and Early Post-natal (Amelogenesis)	Enamel hypoplasia; delayed skeletal and dental development.	[7, 11]
Cadmium (Cd)	Cytotoxicity: Induction of oxidative stress in ameloblasts, leading to disrupted protein secretion during the enamel matrix formation phase.	Developmental stages of hard tissue	Osteotoxic effects; reduction in salivary gland function (hyposalivation).	[7]
Particulate Matter (PM <sub>2.5</sub> /PM <sub>10</sub> )	Systemic Inflammation: Triggering of systemic inflammatory cytokines (e.g., IL-6, CRP) that may compromise oral mucosal immunity and promote an acidic oral environment via mouth breathing.	Chronic exposure throughout adolescence	Periodontal inflammation; dry mouth (Xerostomia); respiratory-linked oral dryness.	[14]

PM<sub>2.5</sub> and nitrogen dioxide (NO<sub>2</sub>) has emerged as a critical variable in HNC incidence. A pivotal retrospective cohort study conducted by Fan et al. (2018) demonstrated a positive correlation between rising concentrations of (NO<sub>2</sub>) and the risk of developing NPC, suggesting that gaseous pollutants may act as direct mucosal irritants or carriers for carcinogenic compounds [33]. Furthermore, this association is not limited to gaseous emissions; research analyzing data from major urban centres has indicated that residents exposed to high cumulative levels of SO<sub>2</sub> and PM<sub>10</sub> exhibit statistically significantly higher incidence rates of nasopharyngeal malignancies compared to those in lower-exposure zones [34]. This correlation points to a mechanism where chronic inflammation and oxidative stress induced by pollutants may accelerate cellular mutagenesis in the upper aerodigestive tract.

Transitioning from general ambient pollution to specific chemical exposures, the role of formaldehyde remains a focal point in occupational oncology. Although the International Agency for Research on Cancer (IARC) has long classified formaldehyde as a Group 1 carcinogen, recent longitudinal analyses have provided more granular data regarding its specific impact on nasopharyngeal tissues. A global analysis of disease burden indicates that despite improved safety regulations, occupational exposure to formaldehyde continues to contribute to a measurable fraction of NPC mortality, particularly in sectors involving textile, wood, and chemical processing [35]. It is important to note, however, that the carcinogenesis of NPC is multi-factorial; environmental pollutants likely act synergistically with viral agents, such as the Epstein-Barr Virus (EBV), potentially reactivating latent viral infections or impairing local immune responses [4]. Consequently, mitigation strategies targeting environmental pollutants could serve as a crucial adjunctive measure in reducing the global burden of head and neck malignancies.

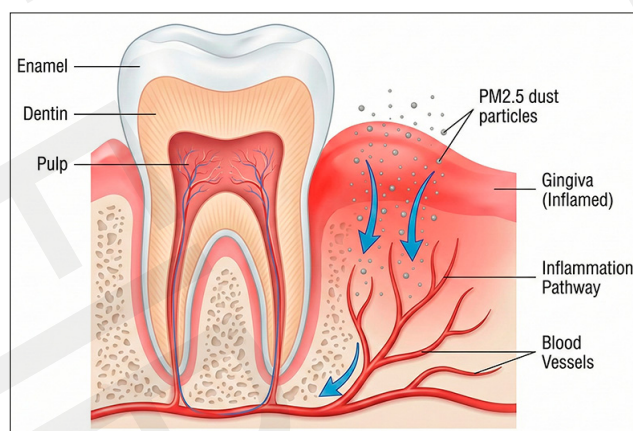
## SUMMARY

Despite the global prevalence of oral pathologies affecting approximately 3.5 billion individuals worldwide, traditional etiological models emphasizing behavioural and microbial factors fail to fully account for the disproportionate disease burden observed in industrializing regions [2, 5]. Consequently, contemporary research advocates for adopting the 'oral exposome' framework, which aggregates cumulative environmental exposures and biological responses throughout

the lifespan to analyze non-behavioural determinants of oral health [3, 21].

This review synthesizes evidence indicating that environmental toxicants, including atmospheric pollutants, heavy metals, and chemical contaminants, function as systemic stressors that compromise oral homeostasis through pluripotential mechanisms [6]. Regarding dental caries, environmental tobacco smoke and heavy metals act as significant modulators; specifically, second-hand smoke suppresses local immune responses and alters salivary buffering, while lead exposure results in enamel hypoplasia through the ionic substitution of lead for calcium in the hydroxyapatite lattice [7, 9, 11]. Similarly, periodontal integrity is compromised by systemic oxidative stress and inflammation triggered by fine particulate matter PM<sub>2.5</sub> and electronic cigarette aerosols, with heavy metals like cadmium accelerating alveolar bone resorption via osteotoxic mechanisms [8, 16, 18].

Furthermore, during critical windows of embryogenesis, maternal exposure to ambient air pollution, occupational solvents, and waterborne disinfection by-products acts as a teratogen for orofacial clefts, an effect often amplified by gene-environment interactions involving variants in folate metabolism such as MTHFR polymorphisms [8, 25, 29, 31]. Longitudinal data also implicate involuntary exposure to gaseous pollutants, including nitrogen dioxide and formaldehyde, in the pathogenesis of nasopharyngeal carcinomas, suggesting these agents function as mucosal



**Figure 1.** Visual representation of the systemic pathway of PM<sub>2.5</sub>-induced periodontal degradation. Inhaled fine particulate matter translocates into the systemic circulation, triggering a cascade of oxidative stress and inflammation that compromises alveolar bone integrity

irritants or carriers for carcinogenic compounds [4, 33, 35]. Collectively, this evidence underscores the necessity of a paradigm shift that integrates environmental risk assessment into preventive dentistry and public health policy to mitigate the synergistic effects of these pollutants on global oral health outcomes [11, 12, 13].

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