

Review

Air Pollution as a Driver of Recurrent Upper-Airway Infections and Comorbid Health Issues

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Abstract

Air pollution represents a critical yet modifiable factor influencing the recurrence and progression of upper-airway infections. This review explores the molecular, immunological, and environmental mechanisms linking airborne pollutants to recurrent sinus and respiratory tract inflammation. Particular focus is placed on pollutant-induced oxidative stress, epithelial barrier disruption, alterations in the microbiome, and immune dysregulation, which collectively heighten disease susceptibility. Integrating recent advances in exposomics, multi-omics, and artificial intelligence, the discussion highlights new approaches to unravel exposure–response pathways and identify predictive biomarkers. Future directions emphasize precision exposure assessment, interventional strategies to improve air quality, and the emerging framework of “clean-air medicine” to guide prevention and policy. Overall, this synthesis underscores the urgent need for multidisciplinary collaboration across environmental science, molecular biology, and clinical research to mitigate the growing burden of pollution-related airway disease and promote sustainable respiratory health.

Keywords: air pollution; upper-airway infections; oxidative stress; immune dysregulation; epithelial barrier; exposomics; microbiome; precision medicine; clean-air medicine

1. Introduction

Air pollution is one of the most significant environmental determinants of global disease burden. Recent estimates suggest that more than seven million premature deaths each year are associated with long-term exposure to polluted air [1]. The respiratory tract, particularly the upper airways, is highly susceptible because it serves as the main point of contact between inhaled pollutants and host tissues [2]. Increasing epidemiological and experimental evidence indicates that recurrent upper-airway infections (UARIs), such as rhinitis, sinusitis, and pharyngitis, can result directly or indirectly from chronic exposure to airborne contaminants [3,4]. These infections, once considered short-term inflammatory responses to irritants, are now understood to involve complex interactions between the immune system and resident microbiota, leading to a gradual transition from acute inflammation to chronic or recurrent disease states [5]. Understanding how environmental pollutants alter mucosal immunity and microbial balance is therefore essential for developing preventive and therapeutic measures to reduce the burden of pollution-related respiratory illnesses.



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Importantly, air pollution-induced inflammation is not limited to the nasal mucosa or upper respiratory tract. Pollutant-driven oxidative stress and immune dysregulation can propagate systemically through the release of reactive oxygen species (ROS), pro-inflammatory cytokines, and circulating inflammatory mediators, leading to endothelial dysfunction and systemic inflammation that affect multiple organs, including the lungs, cardiovascular system, gastrointestinal tract, and central nervous system [6,7]. These interconnected pathways contribute to the development of chronic comorbidities such as cardiovascular disease, metabolic syndrome, and neuro-inflammation, as illustrated in Figure 1.

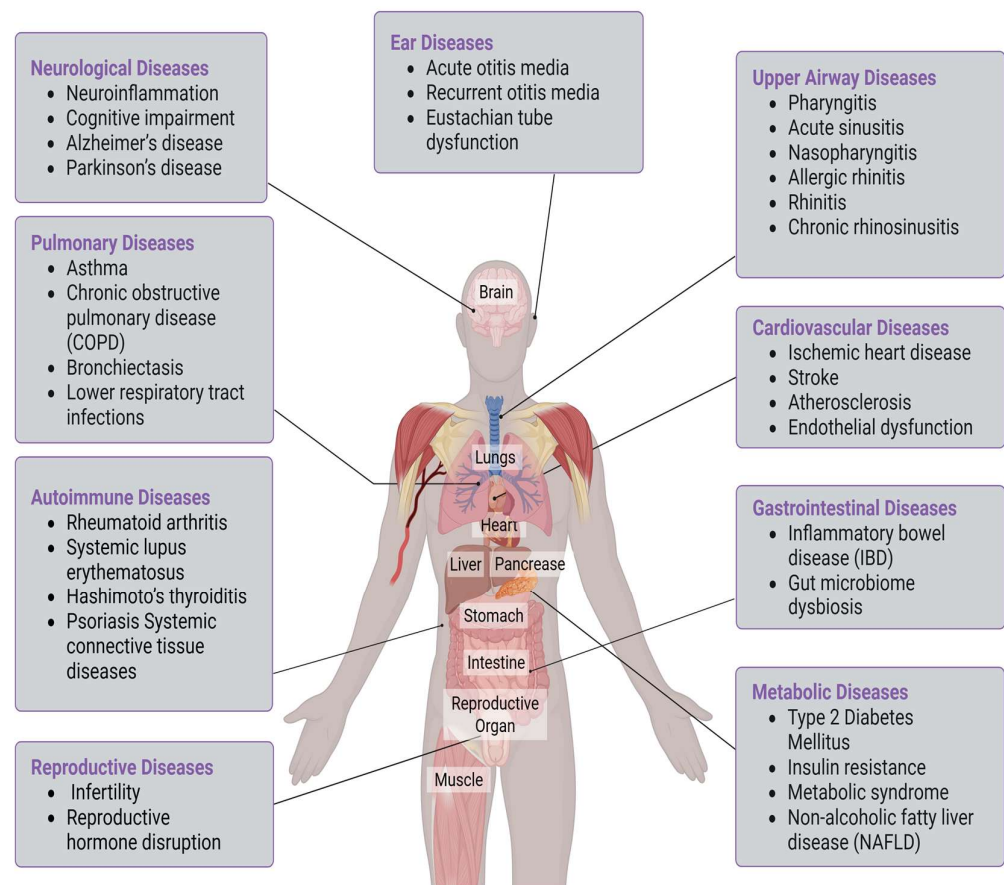


Figure 1. Systemic health effects of air pollution across human organ systems. Chronic exposure to airborne pollutants contributes to recurrent upper-airway infections and triggers systemic inflammatory and oxidative stress responses that extend beyond the respiratory tract. These processes are associated with a wide spectrum of comorbid conditions affecting multiple organs, including neurological disorders (neuro-inflammation and cognitive decline), pulmonary diseases (asthma, COPD, and respiratory infections), cardiovascular disorders (ischemic heart disease and stroke), metabolic diseases (insulin resistance and type 2 diabetes), gastrointestinal disturbances (inflammatory bowel disease and gut microbiome dysbiosis), autoimmune conditions, reproductive dysfunction, and ear-related diseases such as recurrent otitis media. The diagram illustrates the interconnected organ systems involved in pollution-related systemic pathology.

Global industrial expansion, rapid urban growth, and continued reliance on both biomass and fossil fuels have intensified outdoor and indoor air pollution [8]. Outdoor atmospheric pollutants primarily consist of particulate matter (PM_{2.5} and PM₁₀), nitrogen oxides (NO_x), sulfur dioxide (SO₂), ozone (O₃), and volatile organic compounds (VOCs) [9]. In contrast, indoor air commonly contains emissions generated from domestic fuel combustion, cleaning products, tobacco smoke, and biological aerosols. Recent studies have

identified novel airborne contaminants, including microplastics and engineered nanoparticles, embedded within nasal mucosal tissues, indicating their possible involvement in chronic epithelial irritation and local immune dysregulation [10,11]. In many low- and middle-income regions, populations face combined exposure to traffic-related pollutants and biomass-derived particulates, creating a compounded risk that disproportionately affects children, the elderly, and individuals with underlying respiratory disorders [12].

The nasal cavity functions as the primary anatomical and immunological barrier against inhaled environmental agents. Its defense network comprises coordinated mechanisms, such as mucociliary clearance, epithelial tight junctions, and pattern recognition receptors, that detect and respond to microbial or chemical stimuli [13]. Together, these elements help maintain the nasal exposome, which represents total lifetime exposure to environmental chemicals, biological particles, and physical stressors [14]. Continuous exposure to fine particulate matter (PM_{2.5}) and various gaseous pollutants compromises epithelial cohesion, reduces ciliary activity, and promotes oxidative stress, creating favorable conditions for microbial adhesion and subsequent invasion [15,16]. Disruption of the nasal microbiota under pollutant stress, characterized by reduced bacterial diversity and shifts in community composition with increased relative abundance of taxa such as *Moraxella*, has been observed, potentially altering mucosal homeostasis and predisposing to inflammation and infection susceptibility [17]. Findings from recent multi-omics investigations, including transcriptomic and metabolomic analyses, indicate pollutant-specific modifications in epithelial signaling cascades that involve NF-κB activation, cytokine secretion, and lipid peroxidation processes [18].

Accurately quantifying pollutant exposure remains a central challenge in establishing a causal relationship between air pollution and recurrent upper-airway infections (referring to acute infectious conditions affecting the nasal cavity, sinuses, and pharynx). Conventional indicators such as particulate matter concentration, the Air Quality Index (AQI), and chemical composition analyses of pollutants provide valuable population-level insights but often overlook the heterogeneity of individual exposure patterns [19]. Recent developments in mobile sensing technologies, satellite-based spatial mapping, and portable air-monitoring devices have enhanced exposure assessment, enabling near real-time estimation of the inhaled pollutant burden [20]. Artificial intelligence applications are increasingly being employed to merge meteorological, traffic, and clinical datasets, facilitating the prediction of rhinitis and sinusitis exacerbations in relation to pollution peaks [21]. Findings from dose–response investigations indicate a nonlinear association in which sustained low-level exposure induces chronic inflammatory sensitization, thereby heightening vulnerability to microbial infections even when pollutant concentrations remain below established regulatory limits [22].

Epidemiological research consistently highlights the public health significance of the association between air pollution and upper-airway infections. Multiple cohort studies and meta-analyses have demonstrated that elevated concentrations of PM_{2.5} and NO₂ are associated with a higher prevalence of sinusitis, allergic rhinitis, and pharyngitis across different populations [23,24]. Seasonal and geographic factors strongly influence these outcomes, as colder months and temperature inversion events often lead to pollutant accumulation in the lower atmosphere, coinciding with spikes in respiratory infection rates [25]. Individual susceptibility to pollutant exposure is further shaped by socio-demographic factors such as age, sex, genetic background, and socio-economic conditions [26]. Children are particularly at risk due to higher breathing rates relative to body mass and the incomplete maturation of their immune defenses. In contrast, adults exposed for long periods may experience airway remodeling, epithelial thickening, and mucosal fibrosis, which can contribute to persistent inflammation and antibiotic-resistant infections [27,28].

Although epidemiological data clearly establish the connection between air pollution and upper-airway infections, the mechanistic basis underlying pollutant-mediated modulation of host–pathogen interactions remains only partially understood. Airborne particulate matter can act as a physical vector for microorganisms, supporting bioaerosol stability and potentially enhancing microbial adhesion and virulence within the respiratory mucosa [29]. At the cellular level, pollutant exposure alters innate immune equilibrium by suppressing macrophage phagocytic activity, disrupting epithelial signaling, and attenuating interferon-mediated antiviral responses [30]. On a systemic scale, pollutant-triggered cytokine release contributes to neuroimmune communication and chronic low-grade inflammation, which may explain the observed association between recurrent upper-airway infections and metabolic or cardiovascular disorders [31,32]. Integrative research bridging environmental toxicology, microbiology, and immunology is therefore crucial for elucidating the molecular mechanisms linking chronic pollutant exposure to airway infection pathophysiology.

This review aims to elucidate how air pollution drives recurrent upper-airway infections through epithelial damage, immune dysregulation, and microbial imbalance, while emphasizing the need for integrated environmental and clinical approaches to prevent pollution-related respiratory and systemic disorders. An overview of the conceptual framework discussed in this review is provided in the Graphical Abstract (Figure 2).

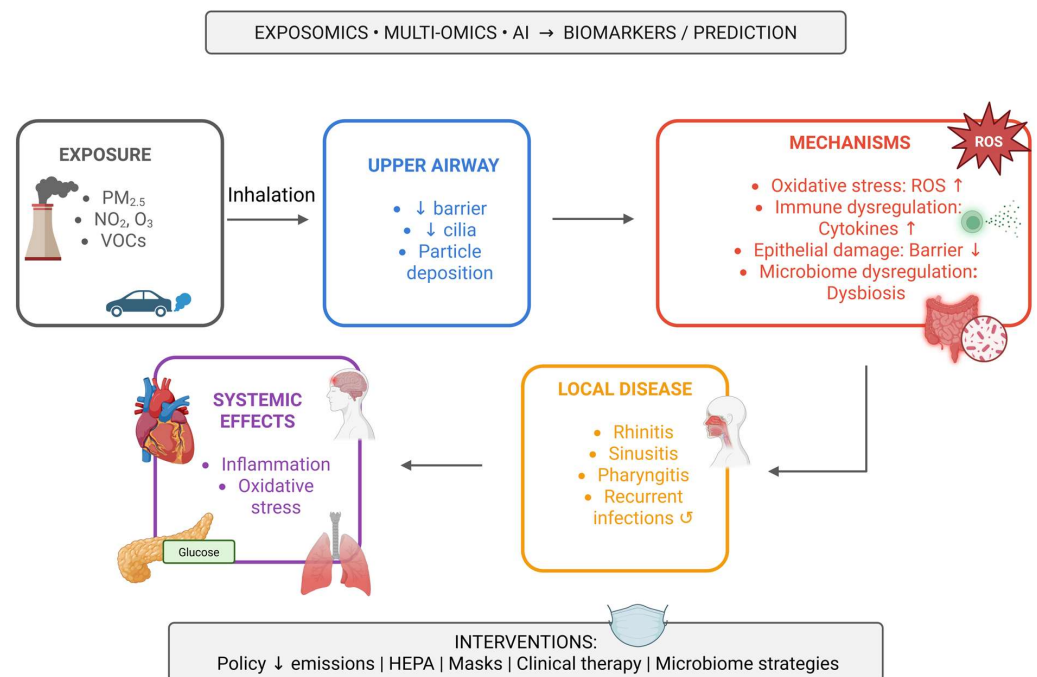


Figure 2. Conceptual framework linking air pollution exposure to recurrent upper-airway infections and systemic effects. Inhaled pollutants (PM_{2.5}, NO₂, O₃, VOCs) impair epithelial barrier integrity and mucociliary function, promoting oxidative stress, immune dysregulation, and microbiome imbalance. These mechanisms increase susceptibility to rhinitis, sinusitis, pharyngitis, and recurrent infections, while also driving systemic inflammatory and oxidative responses affecting multiple organ systems. Exposomics, multi-omics, and AI approaches support biomarker discovery and prediction, with interventions including emission control, filtration, masks, and targeted therapies. Arrows (→) indicate directional progression of processes from exposure to biological effects and disease outcomes, while upward (↑) and downward (↓) symbols represent increased and decreased biological responses, respectively.

This narrative review is based on a targeted literature search of major scientific databases, including PubMed, Scopus, and Web of Science, focusing on studies published primarily over the past two decades. Key search terms included combinations of “air pollu-

tion", "particulate matter", "upper airway infections", "rhinitis", "sinusitis", "oxidative stress", "immune dysregulation", "epithelial barrier", "microbiome", "exposomics", "precision medicine", and "clean-air medicine". Relevant articles were selected based on their contribution to understanding the mechanistic, clinical, and epidemiological links between air pollution and upper-airway disease. Priority was given to recent and high-impact studies. This approach was intended to provide a comprehensive yet non-systematic synthesis of current knowledge in the field.

2. Molecular and Cellular Patho-Mechanisms of the Air Pollution and Immune System Interaction

Airborne pollutants affect the nasal and upper-airway mucosa through various molecular insults that disrupt barrier function, alter innate and adaptive immunity, and remodel the resident microbiota [33,34]. These changes create an environment permissive of repeated viral and bacterial colonization and chronic inflammation. The molecular effects can be grouped mechanistically into overlapping domains: oxidative injury and genotoxic stress; epithelial barrier disruption and mucociliary dysfunction; innate and adaptive immune regulation; and microbiome perturbation with pollutant–pathogen synergy [35].

Oxidative stress and genotoxic injury: Fine and ultrafine particulate matter (PM_{2.5} and nanoparticles) and reactive gaseous oxidants (ozone, NO₂) can generate reactive oxygen and nitrogen species (ROS/RNS) either directly at the epithelial surface, or indirectly by activating resident leukocytes [36]; because of excess ROS, local antioxidant defenses (glutathione, superoxide dismutase's) are overwhelmed which leads to lipid peroxidation, protein carbonylation, oxidative base modifications and single-strand DNA breaks [37]. Redox-sensitive transcription programs (e.g., NF-Kb, AP-1) that prolong pro-inflammatory cytokine production are activated by oxidative stress. On the other hand, oxidative stress disrupts Nrf2 signaling, thereby impairing the adaptive antioxidant response [38]. These together produce a feed-forward loop of perpetual mucosal inflammation and impaired repair. Chronic genotoxic stress additionally advances epithelial cell senescence and atypical repair phenotypes that bias toward remodeling (consistent with goblet cell metaplasia) and a reduced capacity for pathogen clearance [39–41].

Epithelial barrier dysfunction and mucociliary impairment: The nasal epithelium is the principal physical barrier and a coordinated mucociliary escalator [42]. Pollutants disturb intercellular tight junction complexes (claudins, occludin, ZO-1), thereby increasing paracellular permeability and facilitating the release of pro-inflammatory mediators from the epithelium [43]. Concurrently, exposure to pollutants reduces ciliary beat frequency, which can induce ciliary structural injury or ciliated cell loss [44,45]. Chronic exposure to pollutants often induces goblet cell hyperplasia/metaplasia, accompanied by excessive mucin (MUC5AC/MUC5B) production [46,47]. Overall, this leads to the accumulation of hyperviscous mucus, which impedes clearance by retaining pathogens in contact with the mucosa and favoring biofilm formation [48].

Innate immune dysregulation and cytokine imbalance: Air pollutants phenotypically and functionally alter tissue macrophages, dendritic cells (DCs), and airway epithelial sentinel cells [49]. Upon exposure to particulate matter, alveolar and mucosal macrophages exhibit impaired phagocytosis and microbicidal activity, accompanied by decreased secretion of pro-inflammatory cytokines, leading to ineffective pathogen clearance and collateral tissue damage [50,51]. Pollutant components can activate the NLRP3 inflammasome and amplify IL-1 family signaling in epithelial and plasmacytoid DC populations, while simultaneously suppressing antiviral interferon responses, thereby reducing early viral containment and permitting enhanced viral replication [52–55]. Focusing on antigen presentation, DCs exposed to pollutants may display altered costimulatory molecule expression and cytokine

profiles that predispose T-cell differentiation toward Th2 and Th17 pathways. These immune polarities foster allergic inflammation and neutrophilic mucosal injury, respectively, and they are both associated with recurrent and prolonged infection [56].

Adaptive immunity and trained/epigenetic effects: Epigenetic and metabolic changes that can persist beyond the exposure window are imprinted on mucosal immune cells through chronic pollutant exposure. DNA methylation and histone modifications in cytokine and receptor genes modulate responsiveness to subsequent infectious or allergenic stimuli. At the same time, metabolic rewiring in myeloid cells can maintain a trained innate immunity or maladaptive tolerance states that alter host–pathogen dynamics [57,58]. These lasting changes could explain why, during intermittent pollution peaks, prolonged effects on infection susceptibility can be observed [57,59].

Microbiome alterations and dysbiosis: The nasal microbiome is a key component in colonization resistance [60]. Through pollutant exposure, there is a reduction in microbial diversity and selection for taxa capable of surviving oxidative and chemical stressors (often opportunistic pathogens such as non-typable *Haemophilus* and *Streptococcus* spp.) [61]. Microbiome dysbiosis is a promotor of biofilm formation, disruptor of quorum sensing balances, and suppressor of beneficial microbe–host immunomodulatory interactions (e.g., short-chain fatty acid signaling) [62–64]. Biofilms existing within mucus niches are able to tolerate better host defenses and antimicrobials, facilitating chronicity and recurrence [65–67].

Pollutant–pathogen synergy: Pollutant exposure enhances pathogen adhesion, entry and persistence through several mechanisms. Pollutants can increase host cell surface receptors and adhesion molecules utilized by pathogens (e.g., ICAM family members for rhinoviruses) [68–70], upregulate epithelial apoptosis, exposing basolateral adhesion sites [34,71,72], and damage interferon-mediated antiviral cascades [73]. As a vector, particulate matter can carry viable microbes or viral particles, thereby enhancing local inoculum [74–77]. Together, impaired clearance, immune suppression of antiviral defenses, and increased pathogen adherence create an environment permissive of increased initial infection and the promotion of recurrent or prolonged infection courses [68,71,73].

Taken together, these molecular and cellular irregularities establish a self-reinforcing organization in which environmental insults cause an altered mucosal ecology, ineffective host defenses, and an increased tendency for recurrent upper-airway infections. A proper understanding of these nodes enables the study of mechanistic biomarkers and the development of interventions to restore barrier integrity, restore immune homeostasis, and re-establish a protective microbiome [78]. The principal molecular and cellular mechanisms through which airborne pollutants disrupt mucosal immunity and promote infection susceptibility are summarized in Table 1.

Table 1. Molecular and cellular patho-mechanisms linking air pollution to immune dysfunction in the upper airway.

Pathophysiological Domain	Major Pollutant Triggers	Study Design	Key Molecular Targets/Pathways	Cellular and Tissue Effects	Consequences for Host Defense	References
Oxidative stress and genotoxic injury	Fine and ultrafine particulate matter (PM _{2.5} , nanoparticles), ozone (O ₃), nitrogen dioxide (NO ₂)	Narrative reviews (human, in vitro, in vivo evidence); controlled in vitro experimental study using human bronchial epithelial cells (HBEpC) and THP-1-derived macrophages exposed to ozone; biomonitoring study (plant model: <i>Tradescantia pallida</i>); epidemiological and experimental studies	Excess ROS/RNS generation; depletion of antioxidant defenses (glutathione, SOD); activation of redox-sensitive transcription factors (NF- κ B, AP-1); impaired Nrf2 signaling; upregulation of pro-inflammatory cytokines (IL-8, TNF- α) and proteomic alterations (e.g., AKR1B10)	Lipid peroxidation, protein carbonylation, oxidative DNA base modifications, single-strand DNA breaks; epithelial senescence and aberrant repair; enhanced inflammatory signaling	Persistent mucosal inflammation, epithelial remodeling, impaired innate immune responses, and reduced pathogen clearance	[79–81]

Table 1. Cont.

Pathophysiological Domain	Major Pollutant Triggers	Study Design	Key Molecular Targets/Pathways	Cellular and Tissue Effects	Consequences for Host Defense	References
Epithelial barrier dysfunction and mucociliary impairment	Particulate matter, gaseous pollutants (NO ₂ , O ₃), traffic-related pollutants such as diesel exhaust particles (DEP)	In vitro ALI models (human airway epithelial cells, primary nasal cells); experimental pollutant exposure (O ₃ , DEP, NO ₂); molecular and functional assays	Disruption of tight/adherens junctions (claudins, occludin, ZO-1, E-cadherin); altered ciliary function; increased mucin expression (MUC5AC, MUC5B); activation of alarmin cytokines (IL-25, IL-33, TSLP) and inflammatory mediators (IL-6, IL-8)	Increased epithelial permeability (decreased TEER, increased FITC-dextran flux); reduced ciliary beat frequency; ciliary loss/injury; goblet cell hyperplasia and mucus hypersecretion	Impaired mucociliary clearance, mucus retention, enhanced pathogen colonization and biofilm formation	[82–87]
Innate immune dysregulation and cytokine imbalance	PM _{2.5} , diesel exhaust particles (DEPs), oxidative gases (O ₃ , NO ₂)	THP-1-ASC-GFP reporter cells, primary human macrophages, and BEAS-2B/monocyte co-culture exposed to PM _{2.5} (ROFA, CAPs, SRM 1648a) and DEP (SRM 2975) ± TLR agonists (LPS, flagellin); dose–response (1–250 µg/mL, 6–24 h) with pharmacological inhibitors (MCC950, SIQEL 1.1, IL-1ra, anti-TNF-α, sTNFR1) and Nlrp3 ^{−/−} , Casp1 ^{−/−} models; endpoints: ASC-specks, cytokine ELISA, lysosomal integrity, mitochondrial ROS (MitoSOX), OCR (Seahorse), and ATP assays	Altered macrophage and dendritic cell signaling; impaired phagocytosis; activation of NLRP3 inflammasome (ASC-specks, caspase-1); dysregulated IL-1 family cytokines (IL-1β, IL-18); TNF-α, IL-6, CCL2; TLR4/CD14 signaling; K ⁺ efflux; mitochondrial ROS; P2X7-ATP axis; suppressed type I/III interferon responses	Reduced microbicidal activity; altered antigen presentation; skewed cytokine profiles; lysosomal rupture; mitochondrial ultrastructural damage; impaired ATP-dependent IL-1β release (DEP-mediated sequestration)	Inefficient pathogen clearance, enhanced viral replication, and increased susceptibility to infection; enhanced viral/bacterial susceptibility and disruption of IL-1-mediated resolution pathways	[88–95]
Adaptive immune polarization	Chronic exposure to airborne pollutants	UPM-activated DCs directly induced Tm proliferation and expansion into mixed Th1/Th2/Th17 effector cells, including IFN-γ+/IL-17+ Th17.1 cells. These effects were largely MHC-II dependent and occurred in both asthmatic and healthy donors, demonstrating that particulate matter can act as both an adjuvant and antigen to drive pro-inflammatory T-cell responses	Altered costimulatory molecule expression on dendritic cells; cytokine-driven T-cell differentiation pathways (Th2, Th17)	Th2-mediated allergic inflammation; Th17-driven neutrophilic mucosal injury	Chronic airway inflammation and prolonged or recurrent infections	[96–100]
Epigenetic and trained immunity effects	Long-term pollutant exposure	Primary human monocytes or alveolar macrophages exposed to PM _{2.5} /DEP (10–50 µg/mL, 7–14 days), rested 5–7 days, then rechallenged with LPS, <i>E. coli</i> , or influenza H1N1; metabolic (2-DG, etomoxir) and epigenetic (GSK-J4) inhibitors used; endpoints: ChIP-seq, ATAC-seq, DNA methylation, metabolomics, cytokines, single-cell RNA-seq	DNA methylation changes; histone modifications in immune regulatory genes; metabolic rewiring of myeloid cells	Persistent alteration of immune responsiveness; trained immunity or maladaptive tolerance states	Prolonged susceptibility to infection even after transient pollution exposure	[101–110]

Table 1. Cont.

Pathophysiological Domain	Major Pollutant Triggers	Study Design	Key Molecular Targets/Pathways	Cellular and Tissue Effects	Consequences for Host Defense	References
Microbiome alterations and dysbiosis	Oxidative and chemical pollutants	Longitudinal study in children (asthmatic/healthy); clean vs. smog days; fecal 16S analysis with diversity and regression linking pollutants to microbiota; FeNO in asthmatics	Reduced microbial diversity; enrichment of oxidative-stress-resistant taxa (e.g., non-typable <i>Haemophilus</i> , <i>Streptococcus</i> spp.); disruption of quorum sensing and SCFA signaling	Biofilm formation, altered host–microbe interactions, impaired colonization resistance	Chronic colonization, recurrent infections, and reduced microbial-mediated immune protection	[111–115]
Pollutant–pathogen synergy	PM-bound microbes, gaseous oxidants	Human bronchial epithelial (Calu-3) cells at ALI model with repeated PM _{2.5} exposure followed by influenza A infection; assessed viral replication, interferon responses, innate pathways, mitochondrial/metabolic function, autophagy, barrier integrity (TEER), and particle uptake	Upregulation of pathogen adhesion receptors (e.g., ICAM family); epithelial apoptosis exposing basolateral adhesion sites; inhibition of interferon signaling	Enhanced pathogen adhesion, entry, and replication; increased local microbial inoculum via particulate carriers	Increased risk of viral and bacterial infection and prolonged disease courses	[116–118]

3. Air Pollution and Upper-Airway Diseases

The upper respiratory tract is a critical interface between the external environment and the host immune system, where microbial equilibrium, epithelial integrity, and immune surveillance interact dynamically. Evidence indicates that long-term exposure to air pollution disrupts the respiratory microbiome, triggering biological changes that increase susceptibility to recurrent and chronic upper-airway infections. This interplay between environmental pollutants, microbial dysbiosis, and host immune dysfunction provides a framework for understanding pollution-associated respiratory disorders and guiding prevention and therapeutic strategies [117].

The nasal and upper-airway microbiome is a diverse community of bacteria, viruses, and fungi that maintains mucosal homeostasis, limits pathogen colonization, and modulates local immune responses [118]. In healthy individuals, genera such as *Corynebacterium*, *Dolosigranulum*, *Staphylococcus*, and *Moraxella* predominate, sustaining this ecological balance [119]. Continuous exposure to airborne pollutants disrupts this equilibrium by directly affecting microorganisms and altering mucosal physicochemical conditions, leading to microbial dysbiosis and increased susceptibility to infection [120].

Fine particulate matter (PM_{2.5} and PM₁₀) adheres to the nasal epithelium, causing structural damage, tight junction disruption, ciliary dysfunction, and excessive mucus secretion [121]. These changes favor opportunistic pathogen colonization and impair clearance of beneficial commensals. Reactive gases such as NO₂, SO₂, and O₃ further exacerbate this effect by generating oxidative radicals that selectively damage protective microbes, allowing stress-tolerant and potentially pathogenic species to proliferate [122]. The molecular and cellular mechanisms underlying pollutant-induced oxidative stress, inflammatory signaling, and tissue injury are summarized in Figure 3. Indoor pollutants, including volatile organic compounds and formaldehyde, intensify microbial imbalance by imposing antimicrobial stress, reducing diversity, and promoting pro-inflammatory taxa [123].

Epidemiological and metagenomic investigations consistently indicate that individuals residing in areas with elevated air pollution exhibit diminished microbial diversity and an increased prevalence of potentially pathogenic genera, such as *Streptococcus*, *Haemophilus*, and *Staphylococcus aureus* [124]. Complementary metabolomic analyses demonstrate a

metabolic reprogramming of the nasal microenvironment, characterized by an accumulation of pro-inflammatory molecules, including lipopolysaccharides, accompanied by a reduction in anti-inflammatory metabolites such as short-chain fatty acids [125]. Together, these alterations compromise mucosal defense mechanisms and sustain a chronic, low-grade inflammatory state, thereby enhancing susceptibility to recurrent upper-airway infections [126–128].

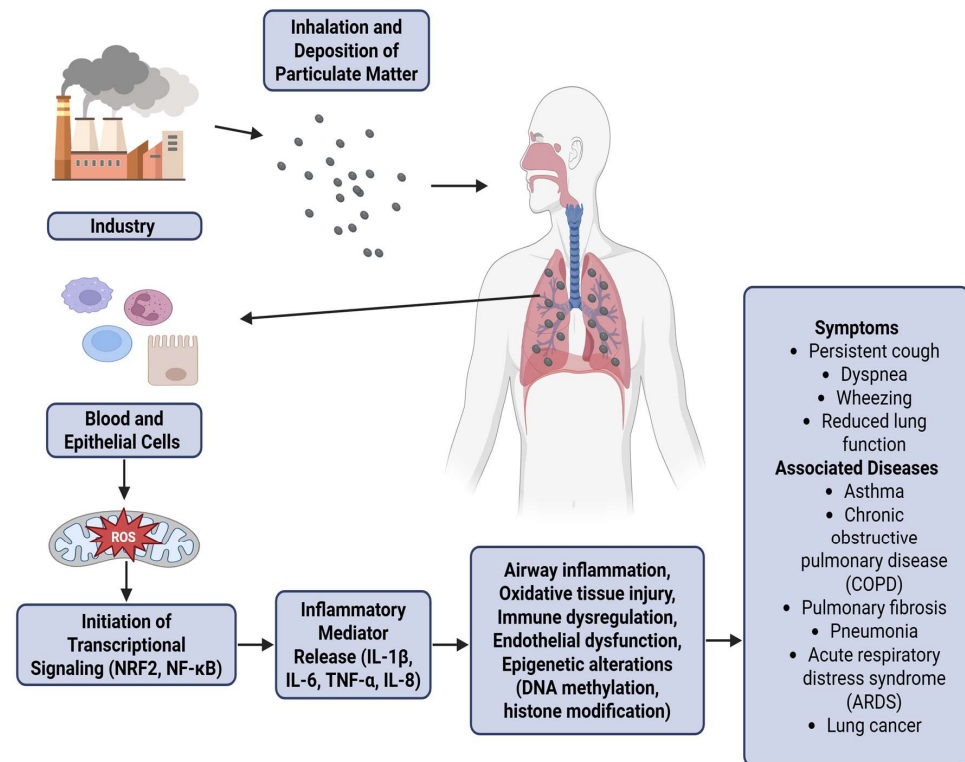


Figure 3. Mechanistic pathways linking particulate matter exposure to respiratory inflammation and disease. Industrial and environmental emissions release particulate matter (PM_{2.5} and PM₁₀) that is inhaled and deposited along the respiratory tract. These particles penetrate airway epithelial surfaces and interact with epithelial and immune cells, leading to the generation of reactive oxygen species (ROS) and activation of transcriptional signaling pathways such as NRF2 and NF-κB. Subsequent release of inflammatory mediators, including IL-1β, IL-6, TNF-α, and IL-8, promotes airway inflammation, oxidative tissue injury, immune dysregulation, endothelial dysfunction, and epigenetic modifications. These molecular and cellular events contribute to respiratory symptoms and the development of diseases such as asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, pneumonia, acute respiratory distress syndrome (ARDS), and lung cancer.

Rhinitis and sinusitis are among the most prevalent inflammatory disorders of the upper respiratory tract. Recent studies show that long-term exposure to air pollutants, particularly PM_{2.5}, PM₁₀, and NO₂, is associated with higher incidence and severity of chronic rhinosinusitis (CRS) [129,130]. Mechanistic evidence indicates pollutants impair epithelial barrier function, mucociliary clearance, and promote sinonasal inflammation [131]. CRS with nasal polyps (CRSwNP), especially eosinophilic T2-high endotypes, appears more strongly linked to pollutant exposure, while CRS without polyps shows weaker associations [132,133]. A large-scale cohort study among Korean adults reported that each 1 µg/m³ increase in PM₁₀ was associated with a 1.22-fold increase in the adjusted odds of developing chronic rhinosinusitis (95% CI: 1.02–1.46) [134]. The upper airway is particularly susceptible as the first barrier against inhaled pollutants, which compromise the sinonasal epithelium by disrupting tight junctions and impairing mucociliary clearance, leading to mucus retention and reduced pathogen elimination. This pollutant-induced inflammation

creates a milieu favorable to chronic pathology, promoting bacterial biofilm formation, nasal polyp development, and mucosal remodeling—hallmarks of chronic rhinosinusitis [135]. Epidemiological data also show that children exposed to high traffic-related air pollution have a higher incidence of allergic rhinitis and subsequent sinus disease [136]. Seasonal and meteorological factors, such as humidity and temperature inversions that trap pollutants, further influence these associations and often coincide with increased sinusitis prevalence.

Otitis media, including both acute and recurrent forms, often arises from nasopharyngeal inflammation and Eustachian tube dysfunction. The nasopharynx, as the interface between the respiratory tract and the external environment, is directly exposed to inhaled pollutants that can impair local immunity, disrupt microbial balance, and compromise mucociliary function. Epidemiological data from Lanzhou, a heavily polluted city in China, show that elevated PM_{2.5}, PM₁₀, NO₂, SO₂, and CO levels are significantly associated with increased outpatient visits for acute otitis media [137]. Mechanistically, pollutants damage the ciliated epithelium of the Eustachian tube, causing mucus retention and creating conditions favorable for bacterial adherence and colonization. This dysfunction contributes not only to the onset but also to the persistence and recurrence of middle-ear infections by sustaining chronic inflammation and microbial dysbiosis [138,139].

Acute upper respiratory tract conditions such as nasopharyngitis, pharyngitis, and tonsillitis are usually episodic, but their recurrent forms contribute substantially to morbidity and healthcare burden. In the oropharynx, airborne pollutants act as direct irritants and modulators of local immune function, compromising mucosal barrier integrity, altering cytokine profiles, and shifting the microbial ecology of the pharynx and tonsils. Epidemiological studies increasingly link prolonged exposure to fine particulate matter (PM_{2.5}) with a higher risk of pharyngitis and tonsillitis, especially in children [140]. Pollutant exposure may reduce the protective activity of commensal streptococcal species, promoting pathogenic bacterial proliferation and increasing infection susceptibility and recurrence [141].

The larynx, an important component of the upper airway, is similarly vulnerable to airborne pollutants, though it has been less extensively studied. Chronic laryngeal conditions such as laryngitis, dysphonia, and vocal cord lesions may be aggravated by pollutant exposure via direct epithelial injury, disrupted local immune responses, and altered microecology. Reactive compounds, including ozone and volatile organic compounds (VOCs), are particularly implicated in laryngeal irritation and inflammation [142,143]. Epidemiological studies further show that populations in regions with high industrial emissions experience increased laryngopharyngeal symptoms, often coinciding with peaks in ambient pollutant concentrations [144–146].

A central feature linking air pollution with upper respiratory tract (URT) disease is its role in promoting recurrence and progression to chronicity. Repeated pollutant exposure sustains mucosal inflammation, impairs epithelial and immune function, and drives microbial dysbiosis, increasing the risk of recurrent infections and chronic disease [147]. Chronic rhinosinusitis, for example, often follows repeated acute episodes in polluted environments and is frequently associated with comorbidities such as asthma and cardiovascular disease [148]. Given the continuity between the upper and lower airways, recurrent URT inflammation may also contribute to lower respiratory pathology and systemic inflammatory responses. Pollutant-induced alterations in epithelial and microbial homeostasis may further extend beyond local effects, linking recurrent URT disease with broader metabolic, cardiovascular, and immunologic complications.

Several epidemiological studies have demonstrated that children living in polluted or urban environments experience higher rates of upper respiratory tract infections (URTIs) and related healthcare visits. This increased susceptibility is primarily due to pollutant-

induced impairment of mucosal immunity and disruption of the microbial balance. Representative studies highlighting these associations are summarized in Table 2.

Table 2. Epidemiological studies reporting increased frequency of healthcare visits for upper respiratory tract infections (URTIs) among children residing in urban or polluted environments.

Author(s) & Year	Study Location/Country	Study Design & Population	Exposure/Pollutant(s)	Key Findings (URTI Focus)
Volkmer et al., 1995 [149]	South Australia/Adelaide	Cross-sectional, parent questionnaire; Preschool children (age 4–5), $n = 14,124$	Indoor fuel type (gas stove, LPG, wood), flueless gas heater, parental smoking	Excessive colds (proxy for URTI): natural gas stove increased risk (OR 1.14); flueless gas heater, wood fire, parental smoking not significantly associated with colds
Ware et al., 2014 [150]	Rural Alaska (2 regions)	Cross-sectional, in-home survey, 561 children in 328 households	Household mold	Household concern with mold associated with elevated prevalence of respiratory infections (OR 1.6–2.5)
Noonan et al., 2012 [151]	Libby, MT, USA	Prospective community intervention; school children surveyed over 4 winter periods; >1100 wood stoves replaced.	Ambient PM _{2.5} from wood smoke (biomass combustion)	Lower PM _{2.5} associated with reduced odds of respiratory infections, including colds [25.4% reduction (95% CI 7.6–39.7%)] and throat infections [45.1% reduction (95% CI 29.0–57.6%)]
Browning et al., 2009 [152]	Seattle, WA, USA (high vs. low ambient wood smoke neighborhoods)	Cross-sectional questionnaire; children aged 1–5 years (subset of total households: 325 high smoke, 257 low smoke); initial + 2 follow-up questionnaires	Ambient wood smoke (PM ₁₀)	A higher prevalence of URTI symptoms was observed in high wood smoke areas. Congestion was more common in the initial survey (46.4% vs. 28.6%) and persisted at follow-up (29.4% vs. 0%), compared with low smoke areas
Honicky et al., 1985 [153]	Not specified (likely US)	Historical prospective study; preschool children ($n = 62$) with matched internal controls (age, sex, town)	Indoor wood-burning stoves	Moderate and severe URTI symptoms (colds, congestion, mild respiratory illness) were significantly greater in children living in homes heated by wood-burning stoves compared with controls ($p < 0.001$)
Van Miert et al., 2011 [154]	Louvain-la-Neuve, Bastogne, Lessines, Belgium (rural and urban mix)	Cross-sectional; adolescents aged ~15 years, $n = 744$	Indoor wood fuel use (heating/cooking)	No increased risk of self-reported URI symptoms with wood fuel use
Hassen et al., 2020 [155]	Legambo District, South Wollo Zone, Ethiopia	Community-based matched case-control; under-five children ($n = 139$ cases, 278 controls)	Type of stove/household fuel, indoor air pollution, ventilation	ARI risk increased with the use of traditional stoves, carrying a child while cooking, and the absence of windows (URTI-relevant factors)
Sanbata et al., 2014 [156]	Addis Ababa, Ethiopia	Community-based cross-sectional study; 422 households with children under 5 years	Biomass fuels (wood, crop residues, dung) vs. cleaner fuels (kerosene, electricity)	A total of 60% of children lived in households that used biomass fuel. Two-week prevalence of ARI: 23.9%. Biomass fuel use is associated with increased odds of ARI (OR 2.97, 95% CI: 1.38–3.87). Kerosene use also elevated risk (OR 1.96, 95% CI: 0.78–4.89).
Dagne et al., 2020 [157]	Ethiopia, University of Gondar Comprehensive Specialized Hospital	Institution-based cross-sectional; under-five children attending the pediatric ward ($n = 422$)	Demographic, hygiene, and residence factors	Prevalence of ARI (proxy for URTI) 27.3%. Significant associations: age < 12 months (AOR = 3.39), maternal age 16–27 (AOR = 1.95) and 28–33 (AOR = 2.73), rural residence (AOR = 2.27), lack of maternal handwashing awareness (AOR = 2.79), lack of meningitis (AOR = 0.22).
Alemayehu et al., 2014 [158]	Gondar city, Ethiopia	Community-based cross-sectional; 715 children under 5 years	Household cooking fuel: high-pollution biomass fuels (wood, dung, straw) vs. cleaner fuels (LPG, electricity)	Prevalence of ARI 26.3%. Children in households using high-pollution fuels: 3.89 times more likely to have ARI (OR = 3.89; 95% CI: 1.54–28.25). Other significant factors: kitchen without windows (OR = 3.53), child playing nearby cooking area (OR = 7.08), child carried on lap/back during cooking (OR = 2.68).

Table 2. Cont.

Author(s) & Year	Study Location/Country	Study Design & Population	Exposure/Pollutant(s)	Key Findings (URTI Focus)
Cai et al., 2021 [159]	21 sub-Saharan African countries	Cross-sectional analysis using Demographic and Health Surveys data; 368,366 children < 5 years for cough	Ambient PM _{2.5} (prior-month average)	Prevalence: cough 20.5%. Overall, no significant association between short-term PM _{2.5} exposure and cough. Slight positive associations in countries with medium-to-high Human Development Index (cough OR = 1.022 per 1 µg/m ³ increase PM _{2.5})
Zheng et al., 2022 [160]	21 cities across China	Systematic review and meta-analysis; children < 18; 33 time-series studies with >18 million outpatient visits	PM _{2.5} , PM ₁₀ , SO ₂ , NO ₂ , O ₃	Short-term exposure to all pollutants is associated with increased outpatient visits for respiratory diseases among children. URTI-specific outcomes were not reported separately.
Oh et al., 2020 [161]	Seven major cities, Republic of Korea	Time-series; children aged 0–3 years	PM _{2.5}	Higher PM _{2.5} associated with increased risk of acute otitis media, particularly in warm season and in children with recent URTI history (RR 1.011 per 10 µg/m ³ increase; RR 1.017 in children with URTI in the prior week)
Martín & Sánchez, 2018 [162]	Madrid, Spain	Ecological study; children attending a Primary Health Care center, 2013–2015; 5125 consultations for URTI	NO ₂ , SO ₂ , CO, NO _x , benzene	Positive correlation between NO ₂ and pediatric consultations for respiratory diseases (including URTIs). The number of consultations is significantly higher when NO ₂ > 40 µg/m ³ . Multiple regression confirmed NO ₂ as the main positive predictor.
Hajat et al., 2002 [163]	London, UK	Time-series analysis of daily GP consultations, 1992–1994; children aged 0–14 years from 45 to 47 family practices (≈268,718–295,740 patients)	SO ₂ , PM ₁₀ , NO ₂ , O ₃ , CO, black smoke	Childhood consultations for URTIs increased by 3.5% (95% CI 1.4–5.8%) per 10–90th percentile increase in SO ₂ . Small positive effects for PM ₁₀ (2.0%, 95% CI –0.2 to 4.2%). O ₃ showed a negative association. Effects are strongest in winter.
Qiu et al., 2018 [164]	17 cities in the Sichuan Basin, China	Multi-city time-series analysis; Children (<14 years), ≈245,899 hospital admissions (all respiratory diseases); 115,788 URTI hospital admissions (all ages)	PM _{2.5} , PM ₁₀ , NO ₂ , SO ₂	Children were more vulnerable to ambient air pollution. A 10 µg/m ³ increase in PM _{2.5} , PM ₁₀ , NO ₂ , and SO ₂ was associated with increased hospital admissions for URTI, with the strongest effects at lag 0–2 days. Air pollution contributed to a measurable fraction of pediatric URTI hospitalizations.
Yu et al., 2023 [165]	82 cities, China	Multi-city longitudinal observational study; children 0–14 years (68.73% of 3,735,934 cases)	PM _{2.5} , PM ₁₀ , NO ₂ , SO ₂ , CO, O ₃	Positive short-term association between NO ₂ , SO ₂ , PM _{2.5} , PM ₁₀ , CO and influenza incidence. Strongest effects: NO ₂ & SO ₂ . The effect is higher in children than in adults. Lag 1–7 days. A substantial attributable fraction of influenza cases due to NO ₂ and CO is higher in northern, polluted cities.
Li et al., 2021 [166]	Shijiazhuang, Xi'an, Nanjing, Guangzhou, China	Multi-city time-series study; children 0–14 years, pediatric outpatient visits for respiratory diseases (ICD J00–J99)	PM _{2.5} (also considered interaction with NO ₂)	Short-term exposure to PM _{2.5} is associated with increased pediatric outpatient visits for respiratory diseases. Strongest effects for URTIs at lag 0. Every 10 µg/m ³ increase in PM _{2.5} : URTIs +0.50% (95% CI: 0.19–0.81%). Cumulative effect (lag 0–7): +0.96% for URTIs. Greater effects in less polluted cities and on lower temperature days.

Table 2. Cont.

Author(s) & Year	Study Location/Country	Study Design & Population	Exposure/Pollutant(s)	Key Findings (URTI Focus)
Yang et al., 2021 [167]	Guangzhou, Shanghai, Wuhan, Xining, China	Multi-city time-series study, children 0–14 years, 183,036 respiratory hospitalizations.	PM _{2.5} , PM ₁₀ , SO ₂ , NO ₂ , CO, O ₃	PM _{2.5} : +2.3% URTI hospitalizations (lag 0–7) PM ₁₀ : +0.8% (lag 0–3) NO ₂ : +2.4% (lag 0–7) SO ₂ , CO, O ₃ : no significant pooled effect Higher risk: children 4–14 years, cold season
Mondal & Paul 2020 [168]	India	Cross-sectional study; 247,743 children < 5 years	Indoor air pollution proxies: biomass cooking fuels, lack of a separate kitchen, and household smoking	Overall, 2.7% of children had acute respiratory infection (ARI) in the previous two weeks. Biomass fuel use increased ARI risk by 10% (OR 1.10, 95% CI 1.01–1.20), absence of a separate kitchen by 22% (OR 1.22, 95% CI 1.14–1.30), and household smoking by 6% (OR 1.06, 95% CI 1.00–1.12). The combined effect of biomass fuel use and no separate kitchen increased ARI risk by 35% (OR 1.35, 95% CI 1.21–1.51).
Woolley et al., 2020 [169]	Uganda (nationally representative survey, 15 regions, urban & rural areas)	Cross-sectional analysis of the 2016 Demographic and Health Survey. 15,405 children under 5 years old in households using wood / charcoal as primary cooking fuel (Urban ~18%, Rural ~82%)	Household air pollution from biomass fuels (wood, charcoal); associated pollutants: particulate matter, CO, NO ₂	Compared with charcoal, wood exposure was associated with higher odds of fever (AOR 1.26, 95% CI 1.08–1.48), cough (1.15, 1.00–1.33), ARI (1.36, 1.11–1.66), and severe ARI (1.41, 1.09–1.85). Urban–rural differences showed higher odds of ARI in urban areas (AOR 1.77), while in rural areas, increased odds were observed for fever (1.23) and ARI (1.27)
Rana et al., 2019 [170]	Afghanistan (nationally representative, 34 provinces, urban & rural areas)	Cross-sectional study; 27,565 under-five children; predominantly rural (77.3%)	Indoor air pollution (IAP) from solid fuel use (SFU): kerosene, coal, lignite, charcoal, wood, animal dung, straw / grass; augmented measure: SFU + kitchen location (indoor / outdoor) to create low-, moderate-, and high-exposure groups	Overall ARI prevalence was 17.6%, higher among solid fuel use (SFU) households (18.7%) compared to non-SFU households (15.2%). High indoor air pollution exposure (SFU with indoor kitchen) was associated with increased ARI risk (aPR 1.17, 95% CI 1.03–1.32). Children in households with indoor kitchens were at higher risk, while rural–urban differences were less pronounced
Khan & Lohano 2018 [171]	Pakistan	Cross-sectional study; 11,040 children under 5 years	Polluting fuels (solid fuels: wood, crop residue, animal dung, charcoal, coal, shrubs / grass / straw; kerosene) vs. cleaner fuels (LPG, natural gas, biogas, electricity)	Children in households using polluting fuels are 1.5 times more likely to have ARI symptoms. Breastfeeding, vaccination, mothers' education, and older maternal age reduce the risk of ARI. Household crowding and a separate kitchen were not significant.
Xu et al., 2022 [172]	25 major cities in China	Multi-city time-series study. Children aged 0–18 years; 97,858 URTI hospitalizations	CO, NO ₂ , SO ₂ , O ₃	Ozone (O ₃) and nitrogen dioxide (NO ₂) exposure were associated with increased upper respiratory tract infection (URTI) hospitalizations, whereas carbon monoxide (CO) and sulfur dioxide (SO ₂) showed little to no effect. Age-specific differences were observed, with children under 1 year being more sensitive to SO ₂ and O ₃ , and children aged 4–6 years more sensitive to CO and NO ₂ . The effects of O ₃ were stronger during the warm season

4. From Upper-Airway Injury to Multisystem Disease: Mechanistic Pathways Linking Air Pollution to Systemic Health

Air pollution exerts a continuum of injury from the upper airways to systemic organs through inflammatory, oxidative, and neuroimmune pathways. Inhaled pollutants, including

particulate matter (PM_{2.5} and PM₁₀), nitrogen oxides, ozone, and heavy metals, initially induce localized inflammation in the nasal and bronchial mucosa, causing epithelial damage and cytokine release that activate downstream immune responses. With chronic exposure, this inflammatory process extends to the lower airways, contributing to diseases such as asthma, chronic obstructive pulmonary disease (COPD), and bronchiectasis. Pro-inflammatory cytokines (e.g., IL-6, IL-1 β , GM-CSF) may enter systemic circulation, promoting persistent low-grade inflammation [173,174]. This “lung-to-blood” axis is associated with neutrophilia, platelet activation, endothelial dysfunction, and impaired tissue perfusion.

Systemic dissemination of inflammatory mediators links air pollution to cardiovascular and metabolic disease. Persistent cytokine release promotes vascular remodeling, oxidative stress, and endothelial activation, accelerating atherogenesis and microvascular injury [175]. Epidemiological studies consistently associate chronic exposure to particulate matter with increased risks of ischemic heart disease, stroke, and insulin resistance. Ultrafine particles (<100 nm) can also penetrate the alveolar–capillary barrier and enter the circulation, where they deposit in distant tissues, enhancing oxidative stress and thrombosis [176,177]. These mechanisms help explain the link between respiratory pollutant exposure and systemic vascular injury observed in population studies.

Emerging evidence highlights a neuro-inflammatory dimension of air pollution. Ultrafine particles can bypass the blood–brain barrier via olfactory neuronal transport, directly reaching the central nervous system. In the olfactory bulb and cortex, they activate microglia and astrocytes, promoting the release of pro-inflammatory cytokines and reactive oxygen species. The pathways by which airborne pollutants access and affect the brain are summarized in Figure 4. Chronic neuro-inflammation is increasingly implicated in the link between long-term air pollution exposure and neurodegenerative diseases such as Alzheimer’s and Parkinson’s disease [178]. Experimental studies further show that particulate matter can act as a “Trojan horse,” delivering adsorbed metals and organic toxins into brain tissue, where they disrupt mitochondrial function and neuronal signaling. This neuroimmune interaction underscores the systemic impact of environmental exposures.

The immunological effects of chronic air pollution extend beyond the nervous and cardiovascular systems to metabolic and endocrine regulation. Persistent inflammation and oxidative stress disrupt adipokine balance, impair insulin signaling, and contribute to metabolic syndrome and type 2 diabetes. Pollutants may also interfere with steroidogenesis and thyroid hormone metabolism, consistent with epidemiological links to thyroid dysfunction. Lymphatic findings further support systemic dissemination, with thoracic lymph nodes accumulating particulate matter over time, reflecting the lungs as a portal of entry for environmental toxins [179].

In addition, prolonged exposure to PM_{2.5} and PM₁₀ has been associated with an increased risk of autoimmune diseases. Large cohort studies report higher incidence of rheumatoid arthritis, systemic connective tissue diseases, and inflammatory bowel disease, while short-term pollutant peaks have been linked to exacerbations of conditions such as Hashimoto’s thyroiditis, lupus, arthritis, and psoriasis [180–182]. Mechanistically, these effects may involve altered T-cell differentiation, increased pro-inflammatory cytokine production, and oxidative and epigenetic changes that promote autoimmunity [183].

Collectively, these findings depict a systemic continuum: what begins as local airway inflammation can evolve into multisystem disease involving vascular, neural, metabolic, and immune networks. The upper airway thus serves not merely as the first site of contact but as the gateway to systemic immune dysregulation. This perspective reframes air pollution as a determinant not only of respiratory illness but also of whole-body health.

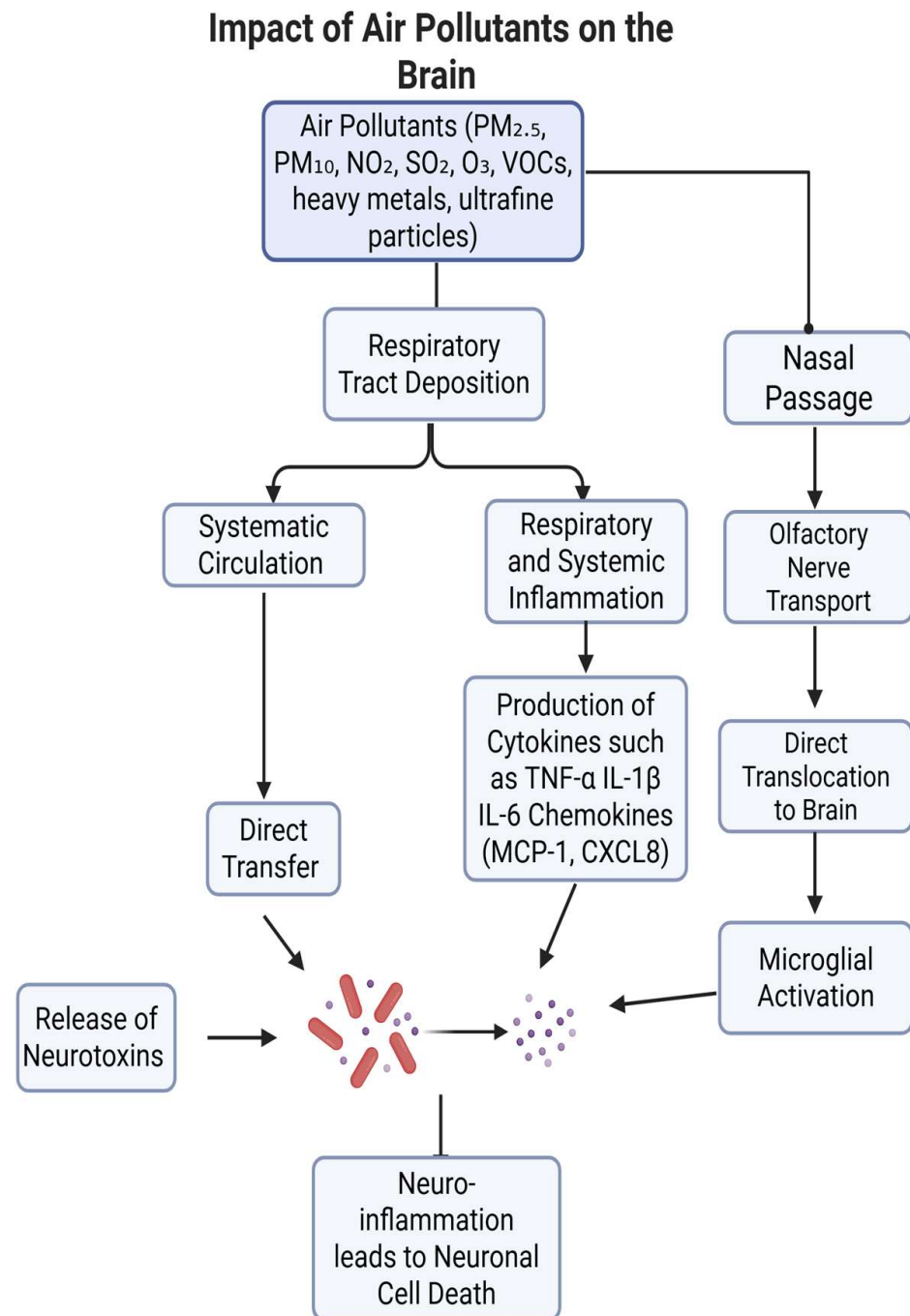


Figure 4. Impact of air pollutants on the brain. Airborne pollutants, including particulate matter (PM_{2.5}, PM₁₀), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), ozone (O₃), volatile organic compounds (VOCs), and heavy metals, can affect the central nervous system through multiple pathways. Following respiratory deposition, pollutants may enter the systemic circulation or induce respiratory and systemic inflammation, leading to cytokine and chemokine release (e.g., TNF-α, IL-1β, IL-6, MCP-1, CXCL8). Ultrafine particles may also access the brain through the nasal–olfactory pathway, enabling direct translocation into neural tissue. These processes activate microglia, promote neuro-inflammation, and ultimately contribute to neuronal injury and cell death.

5. Preventive, Therapeutic, and Translational Strategies

Effective mitigation of the impact of air pollution on recurrent upper-airway infections and comorbid health issues requires a multi-tiered approach spanning population-level prevention, individual clinical management, and translational innovation. These strategies fall broadly into (1) environmental and exposure reduction, (2) individual protective behaviors,

(3) clinical therapeutic interventions, (4) microbiome and immunomodulatory approaches, and (5) translational research and precision medicine pathways. In the following sections, we distinguish between strategies supported by established clinical or epidemiological evidence and those that remain emerging or exploratory, particularly in the context of artificial intelligence, exposomics, and precision medicine.

5.1. Environmental and Exposure Reduction

At the societal level, the foundational strategy for preventing air pollution-related illness is the systemic reduction in ambient pollutant concentrations. This is achieved through multi-pronged policy interventions, including the enforcement of stricter emission standards for industrial and vehicular sources, the strategic implementation of low-emission zones in urban centers, and a transition towards cleaner fuel alternatives coupled with the promotion of electric mobility. The efficacy of such measures is supported by meta-analyses of urban air quality interventions, which confirm that integrated strategies targeting a spectrum of pollutants, particularly particulate matter (PM), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and volatile organic compounds (VOCs), are consistently associated with statistically significant declines in population-level respiratory symptomatology and infection rates. From a pathophysiological perspective, the benefit of improved air quality for the upper airways is direct and multifaceted. Reduced exposure to pollutants mitigates chronic mucosal inflammation, preserves the integrity of the epithelial barrier, and stabilizes the commensal nasal microbiome. This, in turn, diminishes the pathophysiological drivers of epithelial injury and microbial dysbiosis, thereby lowering the population risk for recurrent episodes of rhinitis, sinusitis, and pharyngitis [184–187].

Complementary to systemic policies, targeted exposure-mitigation strategies are essential. Urban green infrastructure, such as vegetative barriers, functions as a passive biogenic filter, improving local air quality. At the individual level, consulting air quality indices to moderate outdoor activity and selecting travel routes distant from high-traffic corridors minimizes personal exposure. Indoors, ventilation, HEPA filtration, and the substitution of solid fuels with clean alternatives (e.g., LPG, electricity) significantly reduce inhalation of combustion-derived aerosols. These measures are particularly critical in high-exposure environments, including low-resource settings with persistent ambient and household air pollution [188].

5.2. Individual Protective Behaviors

When systemic pollution control is inadequate, individual-level interventions provide a critical layer of protection. Evidence supports several exposure-mitigation strategies: monitoring real-time air quality indices to guide the timing and intensity of outdoor exertion, avoiding high-traffic corridors during commuting, and utilizing well-fitted respiratory protection (e.g., N95/FFP2 respirators) to reduce the inhaled dose of particulate matter, particularly for susceptible subgroups. Furthermore, portable air cleaners equipped with High-Efficiency Particulate Air (HEPA) filters consistently demonstrate a capacity to lower indoor PM_{2.5} concentrations and improve subclinical cardiopulmonary endpoints. For upper-airway health, these behavioral and mechanical strategies are paramount. By reducing the total pollutant insult at the primary point of entry, they help preserve essential nasal defenses, including mucociliary function, epithelial barrier integrity, and commensal microbiome homeostasis [189–191]. High-filtration masks (FFP2/N95) can also reduce exposure to airborne allergens, improving nasal and ocular symptoms in allergic rhinitis. However, prolonged use may cause nasal discomfort, dryness, itching, or “mask-induced rhinitis,” likely due to altered airflow, increased humidity, and local irritation rather than true allergic inflammation [192–194].

5.3. Clinical Therapeutic Interventions

In populations chronically exposed to elevated air pollution, the clinical management of recurrent upper-airway infections must be tailored toward mitigating both microbial and pollutant-induced epithelial injury. A comprehensive environmental exposure assessment should be integrated into the clinical history to quantify pollutant burden, occupational risk, and indoor air quality [195,196]. Such contextual data are indispensable for accurate diagnosis and the development of patient-specific preventive strategies.

Clinical management should prioritize minimizing exposure to pollutants and allergens, along with rigorous control of comorbid allergic airway diseases (encompassing both upper and lower airway pathological conditions, including chronic inflammatory disorders). Allergic rhinitis and asthma amplify pollutant-driven oxidative stress and inflammatory signaling via IL-4, IL-5, and IL-13 pathways, rendering the upper-airway epithelium more susceptible to microbial colonization and recurrent infection [197–199]. Hence, simultaneous control of these comorbidities is critical for therapeutic efficacy.

Pharmacologic interventions remain foundational, with intranasal corticosteroids, antihistamines, and topical or systemic decongestants serving as first-line agents. Yet, in high-exposure settings, prolonged or combination therapy is often necessary to suppress chronic pollutant-mediated activation of NF- κ B and related pro-inflammatory cascades. Adjunctive administration of antioxidants (e.g., N-acetylcysteine or vitamin C) has also been explored to counteract reactive oxygen species generated by particulate exposure, though robust clinical validation is ongoing [200–203].

Nasal saline irrigation (isotonic or hypertonic) constitutes a mechanical and biochemical defense strategy. By removing deposited particulate matter and desquamated mucus, it reduces the concentration of cytokines such as IL-8 and TNF- α in nasal secretions, interrupts early biofilm formation, and facilitates mucociliary clearance. Meta-analyses have consistently demonstrated its efficacy in reducing symptom severity and infection recurrence, especially in polluted urban environments [204–207].

5.4. Microbiome and Immunomodulatory Approaches

While the mechanistic links between air pollution, microbiome disruption, and immune dysregulation are increasingly supported by experimental and multi-omics studies, clinical translation of microbiome-targeted therapies remains largely in the exploratory stage. Emerging therapeutic approaches target the disruption of sinonasal microbial communities caused by air pollutants, aiming to re-establish a healthy, resilient microbiome. Interventions involving the topical or oral administration of specific probiotics or prebiotics are under investigation for their capacity to selectively promote protective commensal bacteria, such as *Corynebacterium* and *Dolosigranulum*. The underlying premise is that by fortifying the nasal microbiota, these treatments could enhance mucosal immunity and competitively exclude opportunistic pathogens, thereby lowering the incidence of recurrent infections. Although direct clinical evidence from human studies remains limited, this paradigm is substantiated by multi-omics research that delineates a clear trajectory from pollutant exposure to characteristic microbiome alterations and subsequent disease phenotypes [208–210].

Concurrently, therapeutic strategies to mitigate oxidative stress are being developed to protect the nasal epithelium. The administration of antioxidants via systemic or inhaled routes aims to neutralize reactive oxygen species generated by particulate matter, thereby safeguarding epithelial barrier function and moderating dysregulated immune activation. Recent syntheses of available data indicate that inhaled antioxidant formulations show particular potential to reduce oxidative damage to the airway surface liquid directly. Together, these microbiota-targeted and immunomodulatory approaches constitute a promising new

class of interventions, translating mechanistic insights on pollutant-induced damage into potential clinical solutions [211,212].

5.5. Translational Research and Precision Medicine

While precision medicine approaches integrating multi-omics data and personal exposure monitoring show promise, much of this field remains exploratory, with limited direct clinical validation in upper-airway diseases. A precision medicine approach is emerging and under investigation, utilizing multi-omics data, personal exposure monitoring, and clinical biomarkers to identify individuals potentially at high risk for pollution-associated upper-airway disease. This enables preemptive, targeted interventions like personalized air filtration or microbiome therapy. Research must now prioritize clinical trials with upper respiratory endpoints in polluted areas and conduct cost–benefit analyses of exposure reduction strategies. Such evidence is vital to position upper-airway health as a key metric in air pollution policy [192–196]. However, further research and clinical validation are required before these strategies can be routinely implemented in clinical practice [213–217].

6. Future Outlook and Conclusions

Future research should prioritize integrating precision exposure science with molecular phenotyping. Measuring personal exposure at high resolution and coupling it with longitudinal multi-omics profiling (epithelial transcriptomics, epigenomics, proteomics, metabolomics, and metagenomics) will enable causal analyses at both individual and population levels, facilitating the discovery of biomarker signatures that predict recurrent infection risk [218–220].

Furthermore, there is an urgent need for interventional and natural-experiment study designs. Randomized trials evaluating household and institutional air quality interventions, such as high-efficiency air filtration and clean cooking technologies, should incorporate clinical endpoints and molecular biomarkers of upper-airway disease. These approaches will enhance causal inference and help establish evidence-based mitigation strategies [221–223].

Mechanistically guided therapies represent another key direction. Agents that restore redox balance, enhance mucociliary clearance, or correct immune polarization deserve exploration, alongside microbiome-targeted strategies that restore colonization resistance and disrupt pathogenic biofilms. Precision prevention approaches focusing on high-risk individuals identified through exposomic and genomic risk stratification could further optimize outcomes and efficiency [224–228].

In addition, translational agendas must align with policy and equity frameworks. Since exposure to pollution is strongly influenced by social and environmental factors, clinical and public health efforts should be paired with policies that address emissions reduction, housing quality, and equitable access to clean energy. The adoption of a “clean-air medicine” model—integrating environmental exposure management into clinical practice, prevention, and respiratory care—can serve as a transformative approach [229,230].

Overall, reducing the global burden of recurrent upper-airway infections requires interdisciplinary collaboration across exposure science, molecular biology, clinical medicine, and policy. Emerging advances in exposomics, multi-omics, and AI-driven analytics offer unprecedented opportunities to map the continuum from environmental exposure to molecular mechanism and clinical phenotype. These integrative strategies will enable precision interventions and ultimately promote respiratory health in a pollution-impacted world [231–238].

Air pollution is a measurable and modifiable driver of recurrent upper-airway infections and systemic disease. Mechanistic pathways, including oxidative injury, immune

reprogramming, epithelial barrier disruption, and microbiome imbalance, underlie the persistence of inflammation and repeated infections.

Addressing the global burden of pollution-driven airway diseases demands interdisciplinary collaboration across exposure science, molecular biology, clinical medicine, data analytics, and policy. Advances in exposomics, multi-omics, and artificial intelligence provide new opportunities to trace the trajectory from exposure to clinical outcome, enabling the development of targeted interventions and sustainable preventive strategies. By combining mechanistic insight with public health action, it is possible to reduce the impact of recurrent airway infections and promote long-term respiratory health worldwide.

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