Environmental exposure to air pollution and climate: Intersecting the impact on ear and nose health and chemosensory function (Review)

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Abstract. Air pollution, an emerging global environmental issue, alongside extreme meteorological conditions exacerbated by climate change, threaten the sustainability of modern society and contribute to the onset and progression of various ear and nose diseases. Nonetheless, the impact of these environmental factors on ear and nose diseases and related dysfunctions remain inadequately explored. The present review involved a comprehensive search of PubMed, Web of Science, the Cochrane Library and Embase for relevant epidemiological and experimental data. How environmental factors contribute to olfactory and auditory system dysfunctions as well as the potential underlying mechanisms from the perspectives of immunity and inflammation were examined in the present review. It was found that air pollution and meteorological factors significantly influence the prevalence of major ear and nose diseases, including allergic rhinitis, otitis media and sudden sensorineural hearing loss. Of note, the present review also provides an examination of the interaction between severe acute respiratory syndrome coronavirus 2 and environmental factors in ear and nose diseases, highlighting how environmental stressors may worsen disease progression. In conclusion, the present review underscores the burden of multimorbidity caused by air pollution and extreme weather and emphasizes the need for more targeted prevention and management strategies for ear and nose diseases.

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Abbreviations: 25[OH]D_3, 25-hydroxyvitamin D; ACE2, angiotensin-converting enzyme 2; AR, allergic rhinitis; AOM, acute otitis media; AP, atmospheric pressure; CAPD, central auditory processing dysfunction; CNS, central nervous system; COVID-19, coronavirus disease 2019; DCs, dendritic cells; DEPs, diesel exhaust particles; DTR, diurnal temperature range; ENaC, epithelial sodium channel; ET, eustachian tube; ETS, environmental tobacco smoke; EVs, emergency visits; HMEECs, human middle ear epithelial cell lines; Jp-8, jet propellant 8; MUC5AC, mucin 5AC; NETs, neutrophil extracellular traps; NQO1, quinone oxidoreductase 1; NIHL, noise-induced hearing loss; NOS, nitrogen species; O_3, ozone, OM, otitis media; OVA, ovalbumin; PM, particulate matter; RH, relative humidity; ROS, reactive oxygen species; SSNHL, sudden sensorineural hearing loss; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; T-mean, mean temperature; UPM, urban particulate matter; UVB, ultraviolet B; VOCs, volatile organic compounds

Key words: air pollution, meteorological factors, severe acute respiratory syndrome coronavirus 2, ear and nose diseases, mechanisms, epidemiology, oxidative stress, chemosensory dysfunction

Contents

1. Introduction

Ear and nose diseases are often neglected; however, for most patients, the symptoms persist and recur. The low cure rates and high recurrence rates inevitably influence the quality of learning, living and work of patients, particularly of children and adolescents, resulting in significant healthcare costs as diseases progress (1,2). The upper respiratory tract is the first stop in the fight against viral infections and otolaryngological disorders have attracted wide attention, especially after the

sudden outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December 2019 (3). Numerous investigations have reported the etiology, pathogenesis, progression and prognosis of ear and nose diseases, in which air pollution and meteorological factors play key roles (4,5).

Over the past decade, climate change and weather events have gained widespread attention (6). Recent research has established that air pollution has an effect on ear and nose diseases, specifically aggravating these diseases by evoking oxidative stress, exacerbating inflammatory responses and inducing autoimmunity (7,8). Air pollution is currently one of the greatest risk factors for diseases and premature death. Specifically, air pollution (both household and ambient air pollution) caused 6.7 million deaths in 2019, of which ambient air pollution contributed to 4.5 million deaths, an increase from 4.2 million deaths in 2015 and 2.9 million deaths in 2000 (9). Ambient air pollution is primarily caused by particulate matter (PM) and toxic gases. Based on the aerodynamic diameter, PM can be further classified into coarse particles ($\leq$10 μm, PM_{10}), fine particles ($\leq$2.5 μm, $PM_{2.5}$) and ultrafine particles ($\leq$1 μm, PM_1) (10). Toxic gases include CO, black carbon (BC), nitrogen oxides, sulfur oxides and ozone (O_3). The impact of indoor air pollution on human health has gained increasing attention (11,12). A study has shown that indoor dust and bio-super particles are closely linked to the onset of various diseases, with this effect being independent of environmental air pollution (13). Additionally, human activities also significantly influence indoor air quality (14). Research indicates that indoor microbial communities may pose potential health risks (15). Therefore, indoor air pollution is treated as an independent topic of discussion in the present review. Household air pollutants include environmental tobacco smoke (ETS), volatile organic compounds (VOCs) and indoor allergens.

In addition to air pollution, the role of meteorological factors has become increasingly important. Meteorological factors, including temperature, relative humidity (RH) and wind speed increase not only the activity of pathogens but also the susceptibility of the population (16,17). Conversely, meteorological factors and environmental pollution are deeply interrelated. For example, drier and cooler conditions can boost O_3 pollution by enhancing the rate of photochemical production (18). In addition, bacterial communities in indoor air are affected by environmental pollution and meteorological factors. Studies have indicated that airborne bacterial populations may be altered due to the influence of household activities, such as burning scented candles, which leads to significant changes in bacterial diversity (14,15). The interaction between environmental pollution and meteorological factors promotes the onset and exacerbation of ear and nose diseases, particularly allergic rhinitis (AR), otitis media (OM) and sudden sensorineural hearing loss (SSNHL) (19,20). This emphasizes the importance of improving indoor ventilation and surface hygiene to reduce health risks.

To thoroughly analyze the impact of air pollution and meteorological factors on the onset and progression of ear and nose diseases, while considering the comorbidity and holistic characteristics of ear and nose diseases as well as the mechanisms of known environmental factors, the present study provides, to the best of our knowledge, the first review of the interactions between air pollution, meteorological factors and SARS-CoV-2 on ear and nose diseases. The present review focuses on ear and nose diseases that are closely associated with inflammatory responses or autoimmunity, including AR, OM and SSNHL. We propose that chemosensory dysfunction (olfactory and auditory impairment) may serve as an early indicator of environmental neurotoxicity, offering a new perspective for assessing the impact of environmental pollution on neurological health. Additionally, the present review explores the effects of environmental factors on sensory organ function from both the olfactory and auditory dimensions with the aim of implementing disease prevention and control through environmental management. The coronavirus disease 2019 (COVID-19) pandemic, as an environmental factor, has imposed a significant economic burden on healthcare systems and exacerbated environmental and climate crises (3,21). The respiratory system is the primary target of SARS-CoV-2 infection. As direct portals for viral infection, the ear and nose may be repeatedly attacked, leading to symptoms such as nasal congestion, runny nose and hearing loss. Therefore, the present review discusses the impact of COVID-19 as a unique environmental factor in ear and nose diseases. The detailed search strategies to identify relevant literature can be found in Tables SI-SIV.

2. Ear and nose diseases in the context of environmental factors

The ear and nose are closely interconnected functionally, with the eustachian tube (ET) playing a key role in this relationship. The ET, located in the petrous bone of the temporal lobe, extends from the anterior wall of the middle ear to the nasopharynx and connects the two structures. The main functions of the ET include ventilation of the middle ear, clearance of secretions and protection against direct sound transmission and pathogenic microorganisms (22). Environmental factors such as air pollution and meteorological conditions can influence the physiological functions of ET and contribute to its dysfunction. For example, exposure to air pollutants can lead to oxidative stress, inflammation and immune response changes, which may impair the ability of the ET to maintain middle ear pressure and clear secretions, creating conditions conducive to infection and inflammation. This dysfunction eventually leads to otological symptoms (23). Therefore, understanding the impact of environmental factors on the physiological systems of the ear and nose is crucial for improving the prevention and management of related diseases such as OM and other middle ear disorders. Tables I and II present the results of population and laboratory studies on the impact of environmental factors on the ear and nose physiological systems.

AR. AR, an inflammatory disease, is an IgE-mediated type 1 hypersensitivity response to inhaled allergens characterized by rhinorrhea, nasal congestion, sneezing and nasal itching (24). AR primarily consists of sensitization and effector phases. In the sensitization phase, the allergen induces a shift in the T helper (Th)1/Th2 balance towards a predominant Th2 response, ultimately stimulating B cells to produce IgE. In the effector phase, IgE mediates the degranulation of basophils and mast cells, releasing various bioactive substances that ultimately trigger allergic symptoms (4).

Table I. Air pollution and meteorological factors in ear and nose diseases.

A, AR

Authors, year	Design	Country	Number of participants	Environmental factors	Linkages of ear and nose diseases to air pollution and meteorological factors	(Refs.)
Wang *et al*, 2016	Questionnaire study	China	36,577	PM_{10}, SO_2, NO_2	The prevalence of AR was positively associated with the concentration of SO_2	(25)
Luo *et al*, 2023	Time-series study	China	178,692	SO_2, NO_2, PM_{10}, $PM_{2.5}$, O_3, temperature, humidity and wind speed	Increased concentration of SO_2, NO_2, PM_{10}, $PM_{2.5}$ and O_3, low temperature, low humidity and high wind speed could lead to elevated outpatient visits for AR	(26)
Burte *et al*, 2020	Cross-sectional study	European	1,408	NO_2, PM_{10} and $PM_{2.5}$	Higher $PM_{2.5}$ exposures were related to increased severity of AR	(27)
Liu *et al*, 2020	Cross-sectional study	China	3,177	PM_{10}, SO_2 and NO_2	Prenatal and postnatal exposure to NO_2 led to a higher prevalence of AR in childhood in thesingle-pollutant model	(29)
Yigit *et al*, 2025	Cross-sectional study	Turkey	204	ETS	ETS exposure was associated with more persistent AR in children	(40)
Wang *et al*, 2021	Questionnaire study	China	40,279	Indoor chemical sources	Redecoration, buying new furniture, cooking with natural gas and burning mosquito coils all contributed to higher prevalence of AR	(11)
Dong *et al*, 2013	Cross-sectional study	China	30,780	ETS	Women exposed to ETS had higher odds of AR (2.33 vs. 1.61%) than those who were not	(42)
Hu *et al*, 2020	Time-series study	China	646,975	Temperature, RH, pressure, precipitation, sunshine and wind speed	Increased incidence of AR in childhood at low RH, low wind speed and high mean air pressure	(62)
Wu *et al*, 2022	Time-series study	China	33,599	Temperature and RH	More outpatient visits for AR in high RH regions	(16)
B, OM						
Belachew *et al*, 2024	Retrospective cohort study	European	2568	NO_2	Exposure to NO_2 during pregnancy and the first year of life increased the risk of ear infections in infants	(84)
Deng *et al*, 2017	Retrospective cohort study	China	1,617	PM_{10}, SO_2 and NO_2	prenatal exposure to SO_2 was positively associated with the onset but not repeated attacks of OM	(85)
Park *et al*, 2021	Time-series study	Korea	169,080	PM_{10} and $PM_{2.5}$	$PM_{2.5}/PM_{10}$ exposure was associated with elevated acute OM onset in children under 2 years of age	(86)

Table I. Continued.

B, OM

Authors, year	Design	Country	Number of participants	Environmental factors	Linkages of ear and nose diseases to air pollution and meteorological factors	(Refs.)
Lu *et al*, 2023	Retrospective cohort study	China	8,689	SO_2, NO_2, PM_{10} and $PM_{2.5}$	Prenatal and postnatal exposure to PM increased the lifetime risk of OM in childhood	(87)
Veivers *et al*, 2022	Cross-sectional study	Australia	2,880	Energy sources used for heating, cooling and cooking, pets and ETS	Gas heating, reverse-cycle air conditioning and pet ownership had a positive association with the lifetime onset of OM	(88)
Nieratschker *et al*, 2023	Time-series study	Austria	1,465	Temperature, RH, pressure, precipitation and wind speed	Exposure to high pressure, low wind speed and high RH could lead to elevated incidence of AOM	(98)
Jiang *et al*, 2023	Cross-sectional study	China	7,075	Temperature and RH	Low RH had a strong effect on the incidence of AOM in preschool-age children	(99)

C, SSNHL

Tang *et al*, 2022	Cross-sectional study	China	12,497	$PM_{2.5}$	SSNHL episodes occurred more frequently in Southern Taiwan, which possesses a higher mean particulate matter ($PM_{2.5}$) annual concentration compared with Norther Taiwan	(109)
Choi *et al*, 2019	Case-control study	Korea	26,000	SO_2, NO_2, PM_{10}, CO and O_3	Episodes of SSNHL were only associated with high concentrations of NO_2	(110)
Tsai *et al*, 2021	Retrospective cohort study	China	64,321	SO_2, NO_2, NO, $PM_{2.5}$ and O_3	Long-term exposure to $PM_{2.5}$, CO, NO and NO_2 all led to a high risk of developing SSNHL	(111)
Chang *et al*, 2020	Prospective cohort study	China	75,767	NO_2 and CO	NO_2 caused SSNHL in a dose-dependent manner	(113)
Lalwani *et al*, 2011	Cross-sectional study	United States	2,288	ETS	The incidence of SSNHL was directly related to the level of ETS exposure	(115)
Seo *et al*, 2014	Retrospective cohort study	Korea	607	Temperature, pressure, RH and wind speed	SSNHL episodes tended to occur more frequently after or in stronger wind speed days	(20)
Lee *et al*, 2019	Time-series study	Korea	817	Temperature, pressure and wind speed	A weak negative association between the mean temperature and SSNHL admissions. Increased mean wind speed, maximum wind speed and daily atmospheric pressure range lead to a higher incidence of SSNHL	(17)

AOM, acute OM; AR, allergic rhinitis; ETS, environmental tobacco smoke; O_3, ozone; OM, otitis media; PM, particulate matter; PM_{10}, coarse particles <10 μm in size; $PM_{2.5}$, fine particles <2.5 μm in size; SSNHL, sudden sensorineural hearing loss; RH, relative humidity.

Table II. Laboratory studies on the effects of air pollution and meteorological factors on ear and nasal diseases and dysfunctions.

Authors, year	Environmental factors	Organ	Conclusion	Qualitative risk assessment[a]	(Refs.)
Piao *et al*, 2023	PM	Nose	Exposure to $PM_{2.5}$ can activate the NF-κB signaling pathway, leading to an increase in the levels of GATA3, RORγ, IL-4, IL-5, IL-13 and IL-17 as well as a reduction in the production of Th1-related cytokines, IL-12 and IFN-γ.	+	(7)
Lubitz *et al*, 2010	PM	Nose	DEP-PAHs promote allergic responses in sensitized basophils in a non-allergen manner.	+	(50)
Matthews *et al*, 2016	PM	Nose	UPM-DC can induce human memory CD4 T cells to secrete IFN-γ and IL-13 and stimulate the generation of Th2, Th1 and Th17 effector phenotypes.	+	(52)
Lavinskiene *et al*, 2012	Dust mite	Nose	After the inhalation of dust mites, peripheral blood neutrophils exhibit increased chemotactic activity, enhanced phagocytic activity and elevated ROS production.	+	(59)
Heinl *et al*, 2024	Pollen	Nose	Pollen promotes the secretion of cytokines such as IL-4 through dendritic cells and induces the differentiation of Th2 cells.	+	(75)
Montgomery *et al*, 2020	PM	Nose	Organic extracts of $PM_{2.5}$ can increase the expression of genes involved in mucin secretion in mucociliary epithelial cells.	+	(100)
Shi *et al*, 2023	NH3	Nose	Ammonia recruits T cells and activates microglial and astrocytic cells, leading to increased release of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6 and IFN-γ) and decreased release of anti-inflammatory cytokines (IL-4 and IFN-β), resulting in tissue damage and impaired olfactory system function.	+	(166)
Kim *et al*, 2022	PM	Ear	In an acute otitis media mouse model, pre-exposure to DEP intensifies inflammation and lymphangiogenesis.	+	(93)
Song *et al*, 2012	PM	Ear	DEP reduces cell viability, induces an inflammatory response and increases the expression of mucin genes in HMEECs.	+	(94)
Park *et al*, 2014	PM	Ear	UPM can induce characteristic inflammatory responses in the middle ear mucosa and alter gene expression related to inflammation and mucin production.	+	(5)
Lee *et al*, 2021	PM	Ear	PM exposure significantly increases the expression of COX-2 and TNF-α mRNA in middle ear epithelial cells, enhances ROS production, induces an inflammatory response and leads to mitochondrial dysfunction and abnormal motility.	+	(96)

Table II. Continued.

Authors, year	Environmental factors	Organ	Conclusion	Qualitative risk assessment[a]	(Refs.)
			Furthermore, PM induces cell death, thereby decreasing cell viability.		
Sung *et al*, 2019	Virus	Ear	Human cytomegalovirus can induce cochlear inflammation during early auditory development in mice.	+	(120)

[a] '+' indicates a positive correlation. COX, cyclooxygenase; DEPs, diesel exhaust particles; DCs, dendritic cells; HMEECs, human middle ear epithelial cell lines; PAHs, polycyclic aromatic hydrocarbons; PM, particulate matter; $PM_{2.5}$, fine particles <2.5 μm in size ROS, reactive oxygen species; Th, T helper cell; UPM, urban PM; GATA3, GATA binding protein 3; RORγ, retinoic acid receptor-related orphan receptor γ.

Research evidence on air pollution and individuals with AR. The effect of ambient air pollution on the incidence of AR in humans has garnered widespread attention. In 2016, a multicenter epidemiological study of 18 major cities in mainland China found a significant increase in self-reported adult AR in 2011 compared with 2005 and reported that the prevalence of AR was positively associated with short-term outdoor air pollution exposure, especially the concentration of SO_2 (25). A recent retrospective registry study in the Guangdong-Hong Kong-Macao Greater Bay Area (China) observed that each 10 $\mu g/m^3$ increment in the concentration of SO_2, NO_2, $PM_{2.5}$, PM_{10} and O_3 corresponded to a significant increase in the daily number of hospital outpatients with AR by 7.69, 2.43, 1.84, 1.55 and 0.34%, respectively (26). Two additional studies based on the European Community Respiratory Health Survey and the Epidemiological Study on the Genetics and Environment on Asthma revealed that higher $PM_{2.5}$ exposure is related to an increased severity of AR. However, no association was found between air pollution exposure and the incidence of AR (27,28). Possible reasons for this include population heterogeneity and the duration of exposure. Therefore, future studies should gather more comprehensive data and focus on diverse ethnicities and different exposure durations.

Recently, the role of ambient air pollution on human growth and development has attracted considerable attention. A retrospective observational study surveyed 3,177 preschoolers in five districts of Shanghai (China) and indicated that prenatal and postnatal exposure to NO_2 led to a higher prevalence of AR in childhood in a single-pollutant model, an association that remained significant in a multi-pollutant model (29). Similarly, another study that adopted machine learning approaches based on a 14-year follow-up birth cohort revealed that both the dose and duration of prenatal exposure to NO_2 were significant predictors of AR incidence until adolescence (30). These studies suggest that younger individuals require more attention when considering the impact of air pollution on AR onset.

In addition to outdoor air pollution, the home environment is also closely related to the occurrence of AR. Since children spend most of their time indoors, the impact of indoor pollution on the incidence of AR in children has become a growing concern (31). In children, whose immune systems are not fully developed, early exposure to mold may increase the risk of immune responses to inhaled allergens and irritants (32). Specifically, a study on indoor mold exposure has shown that children living in environments with high mold concentrations have a significantly increased risk of developing AR (33). Several epidemiological studies have also indicated that children raised in environments with elevated mold levels are at a higher risk of AR, particularly in those with prolonged mold exposure (34-36). Furthermore, early exposure to mold may affect the development of the immune system, making children more susceptible to allergic reactions, which is closely related to the maturity of their immune systems (37). Additionally, exposure to ETS has been positively correlated with an increased prevalence of AR in children (38-40). Harmful substances in ETS, especially inflammatory factors and oxidative stress reaction products, can damage the upper respiratory tract barrier in children, leading to the development of allergic diseases (40). A study has found that inhaling environmental smoke not only increases the risk of AR in children but may also exacerbate pre-existing allergic symptoms (41). Specifically, a questionnaire study conducted in China showed that behaviors such as home renovation, purchasing new furniture, cooking with natural gas and burning mosquito coils were associated with an increased incidence of AR in children, with a particularly significant impact observed in girls (11). Moreover, another study across seven cities in northeastern China found that girls exposed to ETS had a higher likelihood of developing AR compared with those not exposed (2.33 vs. 1.61%) (42). These findings suggest that the effect of environmental smoke on AR in children involves a complex mechanism that requires further investigation to improve the understanding of its specific pathways.

VOCs, such as chemicals commonly found in paints and furniture, have also been found to increase the risk of allergies in children. These VOCs include harmful substances such as benzene, toluene and xylene, and prolonged exposure may trigger immune responses in children, leading to the development of AR (43). This is particularly true during home renovation or when purchasing new furniture, as the concentration of VOCs significantly increases, thereby raising the risk of children being exposed to these chemicals (44). The impact of these household exposure sources on the health of children may be related to the incomplete development of their immune

and respiratory systems. Children's immune systems are more sensitive compared with adults, making them more susceptible to exposure to indoor pollutants, which increases the likelihood of developing allergic diseases. Particularly in indoor environments, household pollution sources such as mold, ETS and VOCs have a more notable impact on children's health, as they spend a substantial amount of time indoors and are thus exposed to these pollutants more frequently. Therefore, improving the home environment and controlling air quality are crucial for the prevention of allergic diseases in children.

Laboratory evidence of the impact of air pollution on AR. PM from urban air pollution consists primarily of a mixture of carbonaceous cores, organic compounds and metallic compounds and is considered to affect AR through three major biological pathways: Allergy, oxidative stress and inflammation (45,46). PM can enhance allergen sensitization and induce a local inflammatory response in the nasal passages (47). Bowatte *et al* (48) demonstrated that early childhood exposure to traffic-related PM enhances allergic sensitization and the degree of this association increases with increasing age. Castañeda *et al* (49) found that PM possesses adjuvant-like properties and can synergize with allergens to promote the allergic inflammatory response. A recent experimental study in an ovalbumin (OVA)-induced combined AR and asthma syndrome mouse model demonstrated that exposure to $PM_{2.5}$ may increase the levels of GATA binding protein 3, retinoic acid receptor-related orphan receptor γ, IL-4, IL-5, IL-13 and IL-17 and decrease the production of Th1-associated cytokines, IL-12 and IFN-γ, in nasal lavage fluid by activating the nuclear factor κβ signaling pathway, thereby exacerbating nasal inflammatory response (7). Notably, a growing body of research has shown that PM can also induce inflammatory cell infiltration in the nasal cavity, independent of allergens (47,50,51). A previous *in vitro* study suggested that urban PM (UPM) alone stimulates the generation of Th2, Th1 and Th17 effector phenotypes as a source of antigens. Moreover, the study observed a decrease in allergen-specific memory T cell cytokine responses in dendritic cells (DCs) loaded with both the UPM and house dust mites compared with DCs loaded with UPM alone (52). These findings reveal the complex mechanisms of PM in AR development and imply that future studies should consider other coexisting factors.

In addition, Xia *et al* (53,54) demonstrated that exposure to traffic-related PM promotes the expression of the costimulatory molecule Jagged 1 on DCs and other antigen-presenting cells via the aryl hydrocarbon receptor, which is activated by polycyclic aromatic hydrocarbons, a component of exhaust particulates. The studies also revealed that Jagged 1 interacted with Notch receptors on T cells and promoted the differentiation of allergen-specific T cells (Th2 and Th17), leading to allergic airway inflammation, especially upon exposure to PM_1. In addition to T lymphocyte-mediated allergic airway inflammation, PM may also contribute to the release of proinflammatory cytokines, the accumulation of macrophages, eosinophils and neutrophils and the generation of reactive oxygen species (ROS), thereby promoting inflammation both locally and systemically (49,55,56). $PM_{2.5}$ deposits in the alveolar region and promotes the release of inflammatory biomarkers, including TNFα, IL-1β and IL-6 from alveolar macrophages and bronchial epithelial cells, further triggering systemic inflammation (57). Another study further revealed that oxidative stress may be responsible for eosinophilic inflammation and airway epithelial injury, particularly when associated with serious infections (55). Neutrophils not only increase the levels of IL-8, which in turn enhance their recruitment to areas of inflammation but also promote ROS generation. These mechanisms enhance systemic inflammation as well as local inflammation of the nasal epithelium in patients with AR (58-60). A recent *in vitro* study observed that neutrophil extracellular traps (NETs) increase the density and viscosity of nasal secretions and enhance nasal tissue injury in patients with AR. However, the effect of PM on NETs was not uncovered (61). Another study indicated that $PM_{2.5}$, upregulates quinone oxidoreductase 1 (NQO1) through the release of NETs and ultimately aggravates respiratory tract mucus secretion due to NQO1-induced expression of mucin 5AC (MUC5AC) in an OVA-induced murine model. Notably, the authors also revealed that antioxidants may inhibit NET release (Fig. 1) (56).

Epidemiological evidence on the impact of meteorological factors in AR. In addition to air pollution, meteorological factors also affect the number of patients with AR. For instance a low-latitude multi-city study in China revealed that low temperatures, low humidity and high wind speeds can lead to increased outpatient visits for AR. Notably, in a stratified analysis, the study found that adolescents and younger adults were more sensitive to low humidity than children and older adults (26). Similarly, another retrospective study in an area with a humid subtropical monsoon climate found an increased incidence of AR during childhood for children exposed to low RH, wind speed and mean air pressure (62). However, the results of investigations on the effects of RH on AR are inconsistent. For instance, a hospital-based study in Beijing (China) reported more outpatient visits for AR at higher RH levels (16). A study focusing on classroom humidity level in ten North Carolina schools showed that both high RH (>50%) and low RH (<30%) increased the risk of allergic diseases (63). These inconsistencies may arise from various factors, such as differences in study design, regional allergen distribution, environmental confounders and different biological mechanisms by which high and low RH may affect AR.

Environmental pollution and meteorological factors may play a role in the development of AR. High temperature, low humidity and environmental pollution increase the risk of AR caused by airborne pollen (64-66). A study by Wu *et al* (16) indicated that low temperatures and high RH enhanced the effects of air pollution on AR. The study further revealed that each 10 mg/m^3 increase in $PM_{2.5}$ concentration led to an increase in AR outpatient visits by 2.34% at low temperature and 1.82% at high RH.

Laboratory evidence on the impact of meteorological factors on AR. As aforementioned, high-humidity environments facilitate the growth of allergens such as mold (67). *Aspergillus fumigatus* can stimulate human basophils to express B-cell activating factor, which promotes the proliferation and differentiation of B cells, further inducing IgE production and intensifying the immune response to allergens in patients with AR (68). Furthermore, both air humidity and cloud cover thickness can affect the amount of ultraviolet B (UVB) exposure received by an individual. Narrow-band UVB

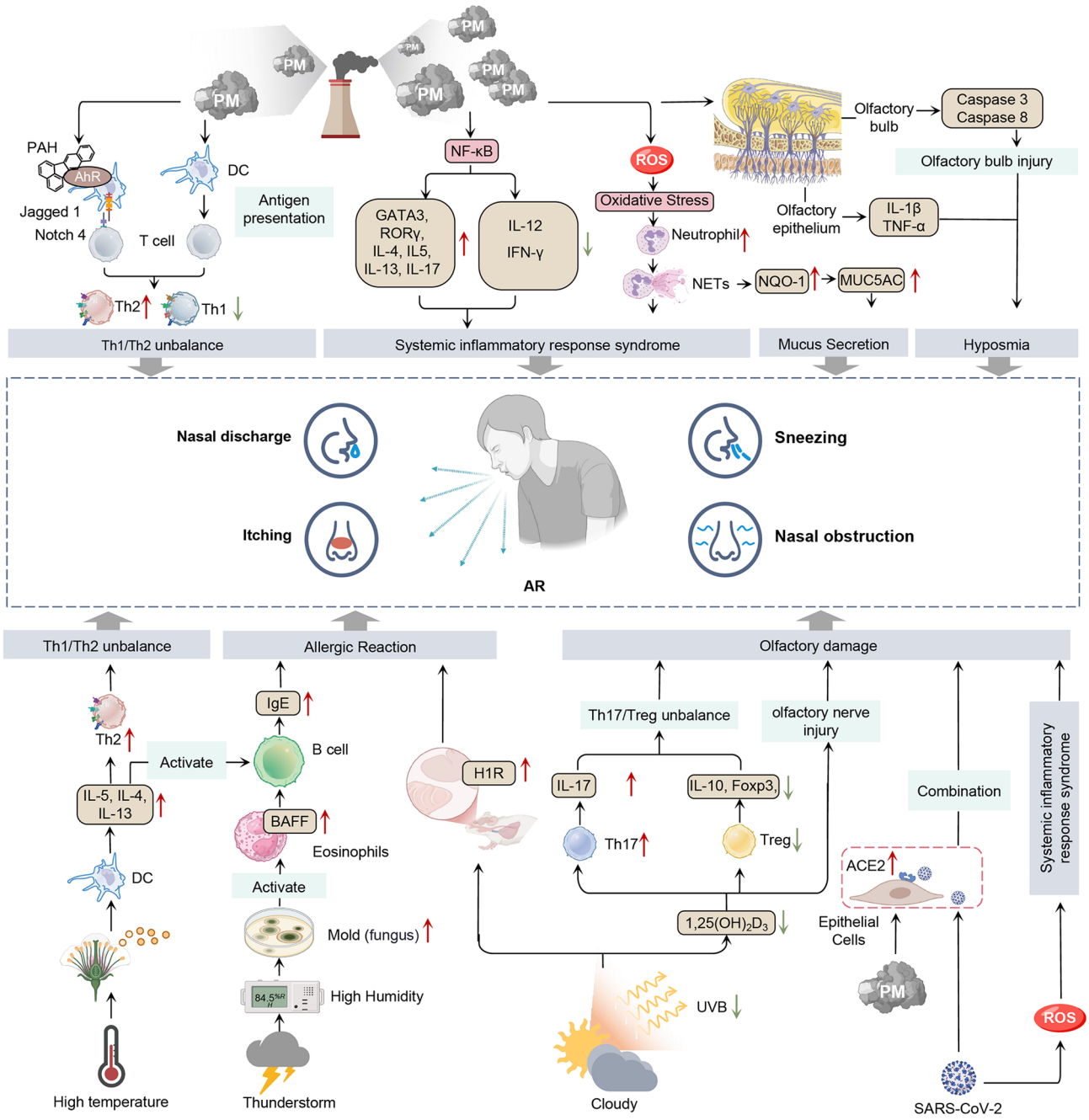

Figure 1. Impact of air pollution and meteorological factors on olfactory function and AR. PM induces Th1/Th2 immune imbalance, enhances systemic oxidative stress and inflammatory responses, thereby leading to olfactory dysfunction and the onset of AR. High temperatures exacerbate the airborne transmission of pollen, further intensifying Th1/Th2 imbalance and allergic reactions. Weather conditions and air humidity affect fungal proliferation, promoting B cell activation and triggering allergic reactions. Furthermore, weather changes influence UVB radiation, thus regulating the Th1/Th2 immune balance. Viruses induce systemic inflammation, further exacerbating olfactory dysfunction and AR. Additionally, viruses can bind to the ACE2 receptors on nasal epithelial cells, leading to olfactory damage, while PM exacerbates this damage by promoting ACE2 expression. 25[OH]D_3, 25-hydroxyvitamin D; ACE2, angiotensin-converting enzyme 2; AR, allergic rhinitis; DCs, dendritic cells; MUC5AC, mucin 5AC; NETs, neutrophil extracellular traps; NQO1, quinone oxidoreductase 1; PAHs, polycyclic aromatic hydrocarbons; PM, particulate matter; ROS, reactive oxygen species; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Th, T-helper; UVB, ultraviolet B; GATA3, GATA binding protein 3; RORγ, retinoic acid receptor-related orphan receptor γ; BAFF, B-cell activating factor.

therapy, based on UVB, has become a routine clinical treatment for AR (69). An *in vivo* study revealed that rats treated with narrowband UVB exhibit significant downregulation of H1R gene expression in the nasal mucosa (70). H1R is associated with allergic diseases, and H1R antagonists have become the first-line treatment for AR (71,72). Thus, the inhibitory effect of UVB on AR may primarily result from modulation of H1R expression in the nasal mucosa. High temperatures can also accelerate the spread and range of pollen in the air. Pollen is a common allergen widely studied for its effects on allergic diseases. Previous studies have found that in the context of AR, pollen can induce DCs to secrete immune regulatory factors, such as IL-5 and IL-13, thereby enhancing the differentiation of Th2 cells (73-75). Additionally, IL-5, IL-4

and IL-13 promote B cell activation and IgE secretion, thereby exacerbating the onset of AR (76).

Results from evidence-based medicine suggest that low levels of vitamin D may increase susceptibility to AR (77). A meta-analysis revealed that *in vitro* vitamin D supplementation alleviated the symptoms of AR (78). Although direct evidence is lacking, a study on allergic diseases found a positive correlation between increased exposure to solar radiation and decreased incidence of allergic diseases in children. Furthermore, providing vitamin D supplements to mothers during pregnancy can modify the association between meteorological exposure patterns and allergen sensitization of children (79). Although few intervention studies are available, it is reasonable to conclude from existing research that a potential link between 'environmental factors-vitamin D-AR' is possible and that supplementation of vitamin D could serve as a potential preventive strategy for AR.

OM. OM is a common infection in early childhood and is particularly prevalent among children under the age of 3 years (80). OM not only affects children's hearing but may also be associated with hearing loss in older adults. A study has shown that hearing loss is linked to age-related cognitive decline and prolonged hearing problems may exacerbate the health burden in the elderly (81). A major consequence of recurrent OM is conductive hearing loss, which affects the development of speech, language, balance and learning abilities, while imposing a notable economic burden on healthcare systems (82,83).

Evidence from population studies on the impact of air pollution on OM. Increasing evidence suggests that environmental pollution plays a notable role in OM onset. A 2024 European birth-cohort study observed a dose-response relationship between prenatal and early-postnatal exposure to traffic-related air pollution (such as NO_2) and the risk of ear infections (including OM) in infants (84). Another retrospective cohort study conducted in Changsha (China) revealed a correlation between prenatal exposure to SO_2 and the occurrence of OM (85). Additionally, the effect of PM on OM has attracted increasing attention. A retrospective study based on data from the Korean National Health Insurance Service indicated that exposure to $PM_{2.5}$/PM_{10} was associated with the incidence of acute OM (AOM) in children under the age of 2 years, with every 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration corresponding to a 4.5% increase in the relative risk of AOM (86). Notably, the study found that $PM_{2.5}$ and PM_{10} had the most significant negative effects on children under 2 years, typically occurring on the day of exposure. Besides, a combined cross-sectional and retrospective cohort study in Changsha (China) indicated that prenatal and postnatal exposure to PM increased the lifetime risk of OM in childhood and further revealed a cumulative effect of $PM_{2.5}$ exposure during the 9 gestational months and PM_{10} exposure during the early post-natal period on OM development (87). Similarly, a retrospective study using time-series analysis showed that exposure to $PM_{2.5}$ within 5 days led to an increase in the incidence of AOM in children aged 0 to 3 years, this association was more pronounced during the warm seasons and in children with a history of upper respiratory infections (47).

Compared with outdoor air pollution, indoor air pollution may have a greater impact on the incidence of OM, particularly given that children spend most of their time indoors. A recent national cross-sectional study on Australian children found a positive correlation between indoor environmental factors (such as the use of gas heating, reverse-cycle air conditioning and pet ownership) and the lifetime risk of OM (88). Another retrospective cohort study in China indicated that postnatal exposure to indoor renovations (such as new furniture and redecoration) significantly increased the lifetime risk of OM in preschool children; this association was particularly pronounced in girls (85). ETS, which is a major indoor pollutant, is a critical factor. It is estimated that ~40% of children are exposed to ETS globally (89). Numerous studies have confirmed that ETS is a significant risk factor for OM in children (90,91). Despite the growing body of literature, data is lacking on the control of indoor pollutants. Therefore, proper monitoring of indoor environmental pollution is crucial for preventing OM in children.

Laboratory evidence of the impact of air pollution on OM. Extensive research has been conducted on the pathogenic mechanisms by which PM affects OM. Recent mechanistic research indicates that fine PM influences the onset and progression of OM through several biological pathways such as inflammation, oxidative stress, mucin-gene upregulation and angiogenesis/lymphangiogenesis (92,93). For instance, ultrafine combustion-derived particles (such as DEPs) constitute a significant fraction of fine and ultrafine PM capable of traversing the alveolar-capillary barrier and eliciting systemic inflammatory responses. *In vitro* studies have shown that PM exposure activates inflammatory cytokines (such as TNF-α and IL-1β) and upregulates mucin genes such as MUC5AC and MUC5B in human middle ear epithelial cell lines (HMEECs), resulting in viscous middle-ear effusions that hinder fluid clearance and contribute to both acute and chronic OM (94,95). Using *in vivo* animal models (rats), it has been demonstrated that PM exposure leads to goblet-cell hyperplasia in the ET and middle-ear mucosa, thickens sub-epithelial layers, increases capillary density and angiogenic/lymphangiogenic factor expression (such as VEGF, VEGFC and CD31) and disrupts epithelial sodium channel (ENaC) expression, which is essential for perimucosal fluid absorption and middle-ear homeostasis, thereby suggesting that early ENaC-targeted intervention may have therapeutic potential (5). In addition, a previous *in vitro* study indicated that potential involvement of ROS could be induced by PM in the progression of OM, as it was found that ROS may promote mitochondrial dysfunction and inflammatory responses, thereby leading to HMEEC apoptosis (96). However, clinical evidence supporting the use of MUC5AC and MUC5B as diagnostic or prognostic biomarkers in OM remains very limited. Although mucin expression has been evaluated in respiratory and airway diseases (such as chronic obstructive pulmonary disease and bronchitis) and shown to be associated with disease progression, ear-specific, large-scale clinical studies validating these biomarkers in patients with OM are lacking (97). Consequently, despite their mechanistic importance, these biomarkers have not yet been adopted in routine clinical practice, mainly due to small sample sizes, heterogeneity in design and the absence of standardized assays. Large-scale, standardized clinical

studies are therefore required to assess whether inflammatory, oxidative-stress, mucin- and angiogenesis/lymphangiogenesis-related biomarkers (including MUC5AC and MUC5B) can serve as reliable diagnostic or prognostic indicators in OM management.

Evidence from population studies on the impact of meteorological factors on OM. In addition to air pollution, meteorological factors are associated with the onset and progression of OM. A retrospective observational study conducted in Cuneo (Italy) revealed a distinct seasonal pattern in the incidence of AOM in children, with more emergency visits (EVs) in winter and fewer visits in summer. Moreover, this seasonal pattern was closely related to upper respiratory tract infections (19). Similarly, a recent retrospective study in Vienna found that EVs related to AOM were more frequent in the winter. The study also observed that a 3-day period of cold weather could increase the risk of AOM-related EVs within 1 day of the temperature event (98). Notably, this study and another study found that high atmospheric pressure (AP), low wind speed and high humidity contributed to an increased incidence of AOM (19,98). However, Vienna, which has a temperate continental climate, typically experiences higher AP and humidity during winter; therefore, further statistical analysis is needed to establish causal relationships while controlling for potential confounding effects among meteorological factors. A retrospective cross-sectional study conducted in Shanghai confirmed that RH has a significant impact on the incidence of AOM in preschool children. The study reported that for every 1% increase in RH, the number of AOM-related visits by preschool children increased by 10.84% (99). Given the increasing frequency of weather events due to climate change, further research in other countries and regions is necessary.

Laboratory evidence on the impact of meteorological factors on OM. In addition to air pollution, meteorological factors, including low temperatures and dry air, can increase the risk of AOM. Viral upper respiratory tract infections have been proposed as a possible bridge linking meteorological factors and AOM since AOM is often secondary to acute upper respiratory tract infections (19,100). Cold and dry weather conditions have been shown to reduce nasal mucociliary clearance and lead to fluid loss in the nasal passages and ET, thereby weakening the upper respiratory defense and heightening susceptibility to viral infection (98). Moreover, viruses can trigger nasopharyngeal inflammation and ET dysfunction, which in turn facilitates further invasion by viruses and bacteria into the middle ear, enhances epithelial cell bacterial adherence and colonization and thus promotes the onset and development of AOM (101). Notably, influenza incidence also peaks in the cold, dry winter months, which provides an additional explanation for the high winter incidence of AOM. Notably, PM has been shown to compromise the barrier function of nasal mucosal epithelial cells (100), thereby increasing the risk and severity of upper respiratory tract infections, which inevitably increases the incidence of AOM (102). Cold and dry air further amplify this effect, underscoring the combined influence of air pollution and meteorological factors on OM (103). Beyond temperature and humidity, other meteorological elements such as AP and wind speed may also contribute to OM. For example, high AP may exacerbate negative middle ear pressure under ET dysfunction, facilitating pathogen ingress, whereas strong winds can enhance the spread of PM and viruses (104). Children, due to their higher respiratory rate and anatomical features (notably, a shorter and flatter ET), are particularly susceptible to environmental pollutants and meteorological stresses. This anatomical disadvantage also makes them more prone to developing OM, especially during upper respiratory tract infections (105).

SSNHL. SSNHL is a subset of sudden hearing loss, which is sensorineural in nature and typically defined as a drop of at least 30 decibels (dB) across at least three consecutive audiometric frequencies occurring within a 72-h window (106). Although its incidence remains relatively low (estimated at 5 to 27 cases per 100,000 individuals annually), SSNHL remains a worrying otological emergency that can lead to persistent hearing impairment and tinnitus, imposing notable psychological distress and financial burden on patients (107).

Evidence from population studies on air pollution and SSNHL. Despite considerable research, the complex etiology of SSNHL remains unclear. Recent epidemiological evidence implicates air pollution as a risk factor for SSNHL (108). Additionally, a cross-sectional study in Taiwan observed an increased incidence of SSNHL from 2000 to 2015 and further revealed that SSNHL episodes occur more frequently in Southern Taiwan, which possesses a higher mean $PM_{2.5}$ annual concentration compared with Norther Taiwan (109). Additionally, a case-control study in South Korea examining short-term exposure to various air pollutants, including SO_2, NO_2, O_3, CO and PM_{10}, found that SSNHL occurrence is significantly associated with elevated NO_2 concentrations (110). By contrast, a long-term cohort study combining two large datasets provided strong evidence that chronic exposure to $PM_{2.5}$, CO, NO and NO_2 increases the risk of SSNHL (111). These contradictory findings may be explained by the cumulative time-dependent effect of air pollution on promoting SSNHL. Additionally, recent data indicate that individuals >30 years are particularly sensitive to NO_2 exposure (112). A large epidemiological study conducted in Taiwan revealed a dose-dependent relationship between NO_2 and SSNHL (113). In addition to PM and gaseous air pollutants, the roles of ETS and heavy-metal exposure in SSNHL have also been investigated (114-116). Zinc, as an effective supplement, has been shown to significantly aid in the hearing recovery of patients with SSNHL when used in combination with other treatments (117). However, current research primarily focuses on a limited number of countries and large-scale studies involving diverse ethnic groups and regions are needed to further validate these effects.

Laboratory evidence supporting the impact of air pollution on SSNHL. The exact pathological mechanisms of SSNHL remain unclear; however, possible mechanisms include viral infections, immune-mediated cellular stress responses and vascular occlusion (118,119). PM exposure has been shown to increase susceptibility to viral infections by allowing viruses to reach the inner ear via the bloodstream or other routes, ultimately inducing cochleitis or neuritis (120). Recent experimental evidence demonstrates that $PM_{2.5}$ exposure

significantly alters airway and systemic immune responses, such as impaired innate immunity, disrupted epithelial barriers and skewing of adaptive immunity, thereby facilitating viral infection and propagation (121). After viral invasion, the adaptive immune system is activated, triggering processes including antigenic cross-reactivity, T cell-mediated cellular immunity and regulatory T cell (Treg)/Th17 imbalance in the inner ear; these immune alterations exacerbate inner-ear damage and contribute to the onset of SSNHL (122,123). Notably, large-scale epidemiological data from the COVID-19 era show increased rates of SSNHL and vestibular neuritis following systemic viral infections (21).

The role of PM in neurological diseases has also attracted much attention. Several studies have demonstrated that PM can induce the expression of inflammatory mediators and the generation of ROS and reactive nitrogen species (NOS) in the central nervous system (CNS), resulting in neuroinflammation, lipid denaturation, microglial dysfunction and even blood-brain barrier dysfunction, which may be associated with SSNHL (8,124,125). Notably, under inflammatory conditions, inducible NOS released by inflammatory cells may produce higher and prolonged NO concentrations. Elevated NO levels in the cochlea have been reported to accelerate the uncoupling of gap junctions in Deiters' cells and delay synaptic transmission, both of which can lead to hearing impairment or even deafness (126,127). Endothelial dysfunction-driven microthrombosis is increasingly being recognized as a key feature of SSNHL (128). Exposure to fine PM induces excessive oxidative stress, depletes cellular NO bioavailability and promotes the upregulation of adhesion molecules (such as P-selectin), platelet-activating factors, leukotriene B4 and cytokines, including IL-8, thereby driving endothelial injury and microvascular compromise (129). Notably, blood supply to the cochlea is provided by the labyrinthine artery and lacks collateral circulation. Once thrombosis disrupts microcirculation, it leads to edema, ischemia and hypoxia in the inner ear tissues; this damage might be one reason for hearing loss. In addition to air pollution, strong wind speeds and extreme heat cause viral transmission, which may contribute to the pathophysiology of SSNHL (20) (Fig. 2).

Evidence from population studies on the impact of meteorological factors on SSNHL. Meteorological factors are considered to be involved in multiple neurological diseases (130); however, the role of meteorological conditions as risk factors for SSNHL remains controversial. A retrospective study in Busan (Republic of Korea) reported that increased mean wind speed, maximum wind speed and a wider daily AP range were weakly associated with a higher incidence of SSNHL. The study also found a weak negative association between mean temperature and SSNHL admissions (17). However, a 2024 time-series study from Hefei (China) examining the mean temperature (T-mean), diurnal temperature range (DTR), AP and RH, found that a lower T-mean, higher DTR and all levels of AP were significantly associated with increased SSNHL admissions, whereas wind speed did not emerge as a strong independent predictor (131). Similarly, another hospital-based study observed that SSNHL episodes occurred more frequently on or immediately after days with higher wind speeds (20). However, several investigations have failed to confirm a consistent correlation between meteorological variables and SSNHL (132,133). Furthermore, the seasonal pattern of SSNHL onset remains controversial; some authors have observed a higher incidence in autumn (134,135), whereas others found no clear seasonal imbalances (20,136). These conflicting epidemiological findings do not support any definitive conclusions. According to our analysis of the relevant literature, several factors may have accounted for these results. First, the duration of several studies was too short to evaluate the influence of meteorological factors on SSNHL onset (131). Second, some studies had small samples and some were limited to specific regions, making it easier to draw conflicting conclusions (17). Finally, given the low prevalence of SSNHL, common weather conditions do not allow for significant impacts (20); therefore, it may be more appropriate to focus on extreme weather conditions.

Evidence from laboratory studies on meteorological factors and SSNHL. Although population studies have revealed associations between various climatic factors and the incidence of SSNHL, current research has yet to clearly elucidate the specific molecular mechanisms by which climatic factors alter the incidence of SSNHL. Notably, existing studies have suggested that climatic factors significantly regulate the chemical sensory functions of the ear at the molecular level (137,138). Therefore, analyzing and exploring the impact of environmental factors on ear sensory receptors will provide valuable insights for future research on the relationship between environmental factors and ear disease.

3. Synergistic effects of meteorological factors and air pollution on ear and nose diseases

In recent years, the complex interactions between environmental pollution and climate factors have received increasing attention (139-141). A 2020 study found significant seasonal variations in air pollutants in Beijing. Specifically, the concentrations of $PM_{2.5}$, PM_{10}, SO_2, NO_2 and CO decreased in summer, whereas O_3 concentrations increased. Furthermore, the incidence of nasal bleeding significantly correlated with these pollutant indicators ($P<0.05$) (142). Further research indicated that although air pollutants negatively affect ear and nose health in other seasons, the concentrations of PM_{10}, NO_2 and SO_2 are positively correlated with the number of ear and nose outpatient visits in winter (143). Therefore, analyzing the interaction between meteorological conditions and environmental exposure can help uncover potential pathogenic mechanisms and identify vulnerable populations. Additionally, further research based on this perspective can provide important theoretical support for the development of precise preventive strategies and optimization of public health policies in the context of climate change.

Climate change, due to rising temperatures, changes in precipitation patterns and an increase in extreme weather events, may exacerbate the generation and diffusion of air pollutants. For example, higher temperatures can promote the formation of O_3 (144) and O_3, as an air pollutant, is associated with an increased incidence of OM in children following exposure in pregnant women (145). In addition,

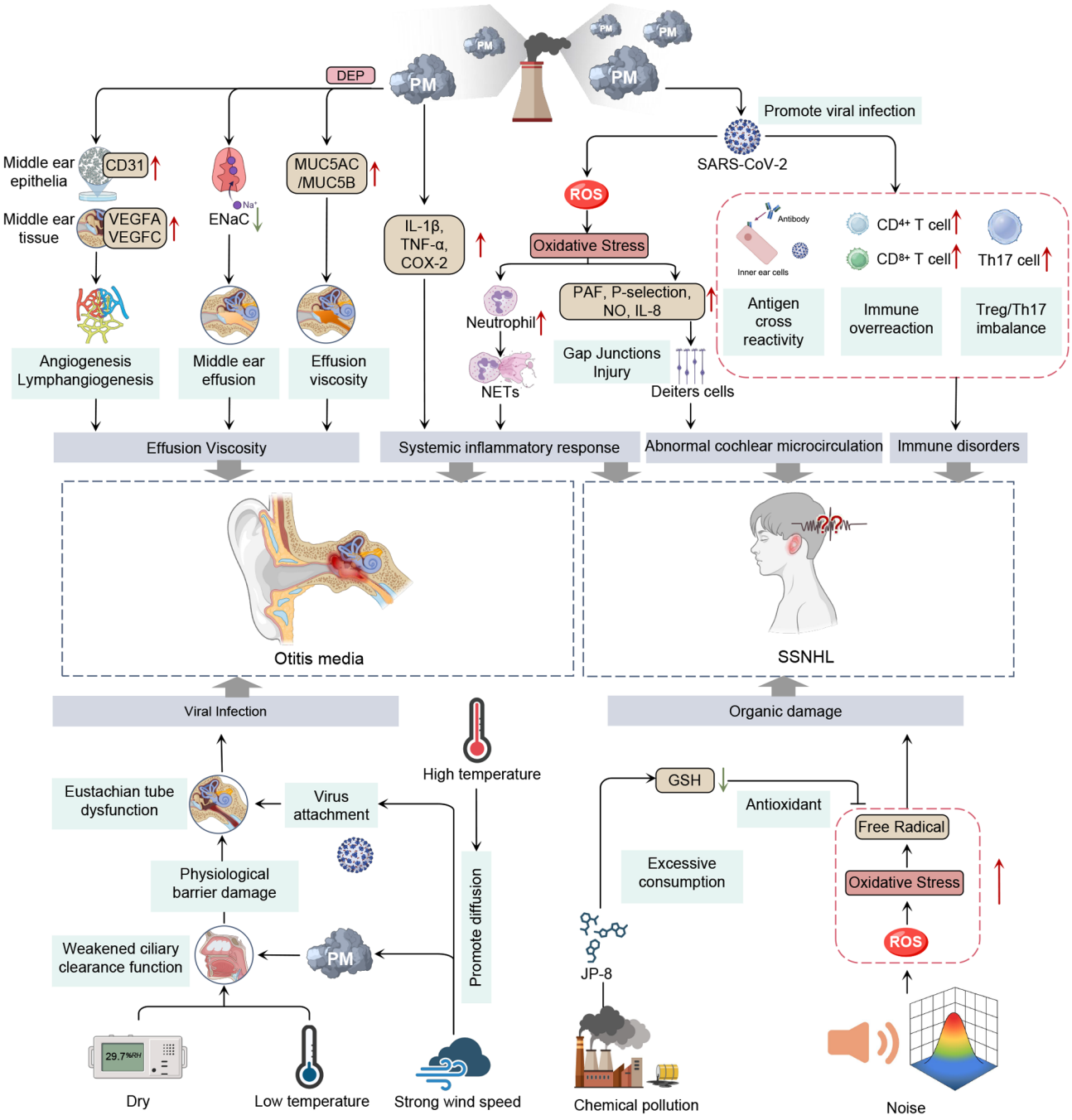

Figure 2. Impact of air pollution and meteorological factors on auditory function and ear diseases. PM can exacerbate middle ear effusion, thereby impairing hearing function. Additionally, viral infections can elevate oxidative stress levels in the ear and induce immune microenvironment dysregulation, further promoting hearing damage and the onset of ear diseases. Air humidity, temperature and viral infections can damage ear structures, thereby intensifying the effects of viruses on hearing function. Strong winds and high temperatures can accelerate the spread of PM and viruses, further aggravating hearing damage. Chemical pollution and noise exacerbate hearing function impairment and the occurrence of ear diseases by increasing oxidative stress levels. COX-2, cyclo-oxygenase-2; GSH, glutathione; MUC5AC, mucin 5AC; PAF, platelet activating factor; PM, particulate matter; ROS, reactive oxygen species; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SSNHL, sudden sensorineural hearing loss; Th, T-helper; ENaC, epithelial sodium channel; DEP, diesel exhaust particle; SSNHL, sudden sensorineural hearing loss; JP-8, Jet Propellant 8.

climate change may alter the diffusion pathways and concentrations of air pollutants (146,147). Strong winds can rapidly spread pollutants and alter their deposition patterns. These changes are particularly significant in areas where urbanization is accelerating. High-rise buildings and narrow streets often create the 'street canyon effect', restricting air circulation and leading to the accumulation of pollutants at localized points (148,149). High concentrations of PM and volatile organic gases directly affect the human ear and nose, increasing the risk of chemical sensory damage (150-152). At the same time, the accumulated high concentrations of PM may also reduce the UVB radiation that reaches the skin surface. UVB has been shown to promote the synthesis of 25-hydroxyvitamin D [25(OH)D_3] in the human body, thereby protecting ear and nose chemical sensory functions (153,154). Strong winds can extend the range of viral

transmission and exacerbate ear and nose diseases. However, environmental pollution, particularly air pollution, industrial emissions and traffic emissions, may affect the rate and pattern of climate change by altering local climate systems. The emission of greenhouse gases, such as carbon dioxide, nitrogen oxides and sulfur oxides is one of the main drivers of global warming (155). The effects of temperature on ear and nose diseases have been reported previously (20,136). Moreover, rising temperatures can exacerbate fungal growth and promote the spread of allergens such as pollen, increasing the risk of allergic diseases. An increased airborne concentration of allergens contributes significantly to the incidence of nasal diseases (32).

4. Chemical sensory functions of the ear and nose

Olfactory. Atmospheric pollution and meteorological variability are emerging global environmental issues that involve complex interactions between specific substances, chemicals and pathogens. Given that olfactory organs are directly exposed to the external environment, various environmental xenobiotics, including chemicals, dust and viruses, constitute important risk factors. Consequently, the olfactory system is a primary biological target of air-pollution exposure (156). A key question is whether pollution exacerbates olfactory decline independently or accelerates age-related degenerative processes. Existing evidence suggests that pollutants may independently affect olfactory function by triggering chronic inflammation, oxidative stress and other mechanisms, and this effect is independent of the aging process (157). However, a study has indicated that the effects of pollution may be more pronounced due to accelerated age-related degeneration, particularly in older populations (158).

Although there are few direct reports on the association between meteorological factors and olfactory dysfunction (159,160), it is not difficult to determine whether meteorological factors, including temperature, sunlight, wind speed, heavy rainfall and humidity, play an important role in olfactory dysfunction. AR can cause swelling of the nasal mucosa, chronic inflammation of the nasal cavity as well as damage to the olfactory bulb and the olfactory nerve, which is an important bridge between meteorological conditions and olfactory dysfunction (161,162). The previous section elucidated the close connection between meteorological factors and AR. In addition, Shin *et al* (153) found that serum 25[OH]D_3 deficiency is significantly associated with olfactory dysfunction in children and that this association is independent of olfactory dysfunction caused by AR. The mechanism can be explained by the following two aspects: First, receptors for 25[OH]D_3 are present in nerve cells and its deficiency can cause olfactory nerve dysfunction, resulting in olfactory decline (154). Second, 25[OH]D_3 reduces inflammation by downregulating the production of the Th17 cell signature, cytokine IL-17, and upregulating the number of IL-10^+ and $Foxp3^+$ Treg cells (163,164). Serum 25[OH]D_3 deficiency may contribute to chronic inflammation in the olfactory neuroepithelium and, thus, olfactory dysfunction. As a precursor of 25[OH]D_3, vitamin D is primarily derived from sunlight (165) (Fig. 1).

Air pollution is categorized into physical (including PM and nanoparticles) and chemical (including DEPs, heavy metals, pesticides and herbicides) pollutants. Andersson *et al* (156) found a statistically significant association between long-term exposure to $PM_{2.5}$ and olfactory identification. When the established model was corrected for age, the association was stronger in older populations. Therefore, the interaction between $PM_{2.5}$ and age significantly affects olfactory discrimination. However, the study did not find an association between short-term $PM_{2.5}$ exposure and olfactory function. The cumulative effects of air pollutants on the olfactory system may result in olfactory loss during aging even at relatively low levels of pollution exposure. Numerous studies have shown that long-term exposure to PM_{10}, SO_2, NO_2, CO, cadmium and ammonia can induce and exacerbate inflammatory responses in the nasal cavity, leading to olfactory dysfunction (166,167). A study by Bernal-Meléndez *et al* (168) showed that repeated exposure to diesel engine exhaust fumes during gestation not only affects fetal olfactory tissues and systems but also influences monoaminergic neurotransmission in the fetal olfactory bulb, leading to altered olfactory behavior at birth. During breathing, due to reduced filtration and clearance by the nasal mucosa, poorer mucosal cilia transport rates prolong PM retention time, which in turn may increase the risk of carcinogenic effects (169). Airborne PM and other pollutants not only contact the olfactory epithelium (OE) and bind to olfactory neurons but can also pass through various abundantly expressed transporters and reach the olfactory bulb via the olfactory nerve. When chemical pollutants attach to ultrafine particles, the resulting complexes are transported across cell membranes via endocytosis. At the same time, the binding of $PM_{2.5}$ to chemical pollutants may put additional stress on the physical structure of the OE, allowing the mixture to reach the CNS through the paracellular pathway as some viruses do, and this binding may also affect the transformation of chemicals in the body (170).

During the COVID-19 pandemic, several studies emphasized the integral role of chemosensory systems in the airborne airways of viruses entering the human body, a pathway that may also be exploited by environmental contaminants (171,172). SARS-CoV-2 virulence may be altered in contaminated areas (169). COVID-19 elicits strong systemic and localized immune responses, leading to the release of cytokines and other inflammatory molecules. These molecules can cross the blood-brain barrier and affect the olfactory system, directly or indirectly causing and exacerbating inflammation and damage to the olfactory neurons (173). A cohort study conducted among young adults in Sweden indicated that long-term exposure to air pollution in living environments was associated with an increased risk of COVID-19 following SARS-CoV-2 infection. The association between exposure to $PM_{2.5}$ and COVID-19 was significantly stronger than that of PM_{10}, BC and nitrogen oxides (174). A recent study has shown that ~80% of patients with long-term COVID-19 still experience olfactory dysfunction 2 years after infection, with some patients continuing to experience complete anosmia, whereas those without apparent anosmia still commonly report a reduction in olfactory function (175). These symptoms are closely related to

changes in the angiotensin-converting enzyme 2 (ACE2) receptor and oxidative stress, supporting the possibility that air pollution and SARS-CoV-2 infection synergistically promote long-term ear and nose sensory dysfunctions (176). ACE2 is widely expressed in the upper respiratory tract and olfactory epithelial cells and acts as the primary receptor for SARS-CoV-2. ACE2 facilitates the entry of the virus and the infection of epithelial cells by interacting with viral spike proteins (177). Population studies have found that individual differences in the response to SARS-CoV-2 are closely related to molecular differences in ACE2 expression (172,178). Furthermore, air pollutants, especially fine $PM_{2.5}$, upregulate ACE2 expression through oxidative stress pathways, significantly increasing the susceptibility of the host to SARS-CoV-2 infection, causing epithelial cell damage and further exacerbating olfactory and gustatory dysfunction (171,179,180). Air pollution may alter the distribution of ACE2 receptors in the olfactory system, making it a more vulnerable target for viral transmission, thereby increasing the risk of olfactory disorders (181). Oxidative stress plays a crucial role in the pathological process of SARS-CoV-2 infection, leading to the production of ROS, which directly damages cells and activates inflammatory responses (182). Air pollutants, such as $PM_{2.5}$, further damage the OE and neurons by inducing oxidative stress, worsening the recovery of olfactory function. Therefore, oxidative stress is considered a key mechanism linking environmental pollution and the sensory dysfunction of the ear and nose caused by SARS-CoV-2. Susceptible factors (including genetic, epigenetic and immune factors), the combined effects of past and current air pollution exposure and SARS-CoV-2 infection may lead to long-term COVID symptoms. Long-term olfactory training can help patients recover their sense of smell to pre-infection levels (173).

Auditory. As a serious public health problem, hearing loss has resulted in growing disease burden, especially among the older population (183,184). Air pollutants and extreme meteorological factors can cause peripheral and central auditory dysfunction and appear to be associated with noise exposure and viral infections (such as SARS-CoV-2), which increase susceptibility to hearing loss through superimposed or synergistic mechanisms.

The potential synergistic effects of noise and air pollution on hearing function have been proposed in multiple studies, and quantitative tests have been conducted to analyze this interaction. For example, a prospective cohort study of 1,179 oilfield workers found that both air pollution and noise exposure significantly increased the risk of occupational hearing loss, both independently and in combination (185). Studies suggest that noise and air pollution may jointly affect hearing function through common biological pathways, such as oxidative stress, inflammation and endothelial dysfunction (186,187). For instance, $PM_{2.5}$, which induces oxidative stress by generating ROS, may cause endothelial dysfunction, which affects the cochlear blood supply and increases the risk of hearing loss (188).

The global climate crisis is worsening and the frequency and severity of extreme meteorological conditions are increasing. The relationship between meteorological conditions and auditory health has become a major epidemiological concern; however, a study has argued that there is no direct relationship (189). We hypothesize that the direct mechanism of auditory impairment may not be meteorological factors, but rather interaction with ototoxic environmental confounders (including environmental pollutants, viruses and bacteria) or exacerbation of pre-existing otological diseases. Specifically, high wind speeds facilitate viral transmission, inducing a systemic immune response that causes SSNHL and central auditory dysfunction. Moreover, inflammation of the upper respiratory tract due to infection can lead to ET dysfunction, which in turn can cause inflammatory lesions in the otological region. As the disease progresses, the tympanic membrane mobility decreases, ultimately leading to conductive hearing loss (190). Under high APs, bacteria and viruses can diffuse further and exacerbate hearing loss. Future studies may need to collect more data, incorporate factors such as upper respiratory infections and explore interactions between multiple weather factors (Fig. 2).

Hydrocarbon fuels contain long-chain and short-chain aromatic and aliphatic hydrocarbons. Epidemiological evidence and animal studies have demonstrated that exposure to jet fuel causes lethality in presynaptic sensory cells, which in turn exacerbates noise-induced hearing loss (NIHL) in air force personnel. This fuel has recently been shown to increase susceptibility to NIHL. For example, the levels of the distortion product otoacoustic emission, a measure of non-linear transduction from outer hair cells, have been shown to be reduced after exposure to Jet Propellant 8 (JP-8), with a no-damage level of 97 dB (no hearing loss or cell death) noise (191). In addition, cytocochleograms plotting the percentage of sensory cell death revealed a significant loss of outer hair cells. Compound action potentials recorded from the peripheral auditory nerve showed that loss of outer hair cells was responsible for permanent hearing loss. A possible mechanism is that JP-8 depletes glutathione both *in vitro* and *in vivo* and the depletion of this important antioxidant increases the likelihood of noise-induced oxidative stress (192). Notably, as reported in a study by Guthrie *et al* (193) that investigated the effect of JP-8 on the development of hearing loss, this fuel might cause central auditory processing dysfunction (CAPD) in normal-hearing Long Evans rats without detectable sensory cell damage, suggesting that CAPD might exist in the absence of hearing loss (194). Therefore, it is recommended that individuals at risk of hydrocarbon fuel exposure undergo an audiological assessment, which should include a conventional audiological assessment in addition to neurophysiological and/or psychoacoustic assessments of the central auditory function. Notably, in a study by Fechter *et al* (195), male rats appeared to be more susceptible to enhanced NIHL from JP-8 exposure. The enhanced sensitivity of male rats to JP-8 and noise may reflect true sex differences in noise susceptibility. However, this might also reflect toxicodynamic factors related to body lipid storage, rather than sexual dimorphism, as male and female F344 rats exhibit significantly different weight gain patterns. Differences in body fat levels between sexes may lead to greater JP-8 fuel stores in male rats, thereby prolonging the duration of the elevated JP-8 body burden (196).

COVID-19 is thought to cause CNS and peripheral nervous system dysfunction. Growing evidence suggests that patients infected with SARS-CoV-2 are at an increased risk for hearing impairment, particularly SSNHL (197,198). A study based on data from visits to tertiary hospitals in China reported an increase in the incidence of SSNHL and tinnitus during the COVID-19 pandemic (3). Another hospital-based study in Eastern India included 452 patients with COVID-19, of whom 28 developed hearing impairment and 24 developed SSNHL (199). Possible mechanisms of hearing loss due to SARS-CoV-2 infection include induction of cochlear microcirculatory dysfunction (200,201), inflammation of the nervous system (including the CNS, peripheral nervous system and auditory centers in the temporal lobe) (202,203) and activation of systemic immune responses due to viral infection (204,205). Furthermore, SARS-CoV-2 causes organ ischemia, tissue inflammation and a hypercoagulable state by inducing endothelial cell inflammation, which may lead to cochlear microcirculatory dysfunction and hearing loss (206). Degen *et al* (207) observed a cochlear inflammatory response on magnetic resonance imaging in patients with hearing impairment complicated by COVID-19 and hypothesized that hearing loss was due to the spread of meningitis to the cochlea as a result of the SARS-CoV-2 infection. In addition, hearing loss increases the risk of depression and anxiety in infected patients (208,209). Early screening of patients with SARS-CoV-2 infection plays a key role in promoting hearing recovery and psychological well-being (207). As aforementioned, pollutants and meteorological conditions increase the risk of OM and SSNHL, thereby causing hearing loss. PM enhances human susceptibility to the virus by damaging the respiratory mucosa and may carry viral particles in conjunction with strong wind speeds to facilitate transmission of SARS-CoV-2. Epidemiological evidence demonstrates that exposure to environmental pollutants increases the incidence of, and mortality from, COVID-19 (210,211). In conclusion, we consider that environmental pollution and meteorological factors may be associated with SARS-CoV-2 infection through synergistic and/or superimposed effects that cause hearing loss (Fig. 2).

Although the present review provides an in-depth exploration of the relationship between environmental factors, SARS-CoV-2 infection and ear and nose diseases, several limitations remain in the current research, particularly regarding population heterogeneity and exposure assessment methods. Individuals of different ethnicities, ages, sexes and socioeconomic backgrounds may have different sensitivities to environmental pollution, which affects the generalizability of the research findings. Moreover, a number of studies rely on environmental air quality monitoring data or self-reported exposure, which may not accurately reflect the actual exposure level of individuals, particularly when pollution sources are complex or exposure varies over time and space. Therefore, future studies should adopt more precise exposure assessment methods, such as personal air quality monitoring and biomarker analysis, to improve the accuracy of assessments and account for the effects of long-term exposure. This will help provide an improved understanding of the relationship between environmental factors and diseases.

5. Conclusions

To the best of knowledge, the present review provides the first systematic comprehensive examination of the interactions among air pollution, meteorological factors and SARS-CoV-2 in ear and nose diseases, filling a critical gap in the literature. We propose that chemosensory dysfunction (olfactory and auditory impairments) may serve as an early indicator of environmental neurotoxicity, offering a novel perspective on how environmental pollution can affect the nervous system. The present review highlights the complex roles of environmental factors in diseases such as RH, OM and SSNHL, emphasizing the need for further research on these interactions. Despite existing research, several unknowns remain that warrant future studies focusing on: i) Longitudinal research, to explore the cumulative effects of long-term exposure to air pollution and meteorological changes; ii) molecular mechanisms, to elucidate how these factors induce diseases through immune and inflammatory pathways; and iii) mitigation strategies, to reduce the impact of these environmental factors through environmental management, personal protective measures and policy interventions.

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Authors' contributions

YCZ and PTZ made significant intellectual and technical contributions, including conceptualizing the study, conducting the initial literature review, refining the core content and designing the manuscript structure. In addition, YCZ and PTZ created the figures and formatted the references using appropriate software. LZ, ZHX, WJZ and MF contributed to data curation and writing the original draft. YXH and YCL contributed to organizing tables, conducting preliminary literature reviews and investigating of the innovative positioning of this manuscript. YHL contributed to conception, supervision and writing/revising the manuscript. Data authentication is not applicable. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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