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BRIEF REPORT



World Trade Center-related asthma: clinical care essentials

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ARSTRACT

Asthma is defined as a heterogeneous disease with respiratory symptoms (wheeze, shortness of breath, chest tightness and cough) that vary over time and intensity, and variable expiratory airflow limitation. Environmental and occupational exposures contribute to its causation. WTC-related or aggravated asthma is considered a World Trace Center (WTC) Health Program certifiable disease. Criteria include defined exposures to the WTC dust and fumes, the presence of symptoms, or aggravated symptoms that are present within 5 years after the last potential for WTC dust/fume exposures (the last 9/11 exposures occurred on July 31, 2002), and a WTC-provider diagnosis of asthma. Asthma is the 3rd most common non-cancer certification among WTC responders and survivors. In this review we provide evidence-based information on the evaluation, diagnosis, and treatment of patients with WTCrelated or aggravated asthma and include peer-reviewed research findings in WTC-exposed populations.

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World Trade Center; environment; adults; air pollution; asthma; dust; workers; occupational lung disease; particulate matter

Introduction

Acute and chronic exposures to World Trade Center (WTC) dust and fumes contribute to the causation and aggravation of asthma in WTC responders and survivors (local workers, residents, students, those passing by on 9/11). In this review we provide evidence-based information on the evaluation, diagnosis, and treatment of patients with potential for WTC-related or aggravated asthma and include peer-reviewed research findings in WTC-exposed populations. This is one of a series of papers for the diagnosis and treatment of persons with WTC-related diseases.1

Relevant WTC exposures

The \sim 1.2 million tons of dust generated by the collapse of the WTC towers had a unique composition with potential for massive acute and chronic exposure dose. Most studies of the dust composition are based on settled dust, as local monitors for airborne particles were destroyed. Over 90% of the settled dust was >2.5 µm aerodynamic diameter. Although less than 1% of the settled dust was in the fine size range ($<2.5 \,\mu\text{m}$), the quantity of the dust resulted in significant airborne concentrations of fine dust.²⁻⁵ Coarse

particles in the WTC dust are more likely to deposit in the upper airways, however the massive quantity of dust resulted in appreciable penetration in the conducting as well as smaller airways, alveoli and interstitium of the lungs. 2,6-8 Importantly, the settled WTC dust was highly alkaline.² Exposure dose analyses for WTC responders and survivors are complex, due to differences in acute exposures (i.e., arrival times, dust cloud exposure), as well as chronic exposures (e.g., prolonged work efforts, incompletely cleaned workplaces, homes or schools, resuspended dust, and fumes).

Asthma as a WTC-certified condition

The biologic plausibility for the development of asthma and the clinical and epidemiologic studies in responders and survivors resulted in the inclusion of asthma or aggravated asthma as a condition certified for health coverage by the WTC Health Program. 9-20 WTC-related asthma is the third most common noncancer certified condition in the CDC-NIOSH WTCHP.²¹ To certify a patient for asthma and asthma treatment, a WTC-3 application must be submitted for a patient whose WTC exposure was substantially likely to have caused, aggravated, or contributed to the diagnosis. To be certified, the WTC Health



Program member must meet 9/11 exposure requirements²² and lower respiratory symptoms must have had an onset within 5 years after the last date of the 9/11 exposure (the last 9/11 exposures occurred on July 31, 2002).²³

Asthma guidelines for diagnosis and management

Major guidelines have been published for asthma and severe asthma. For this best practices article, the selected guidelines are the NIH Expert Panel report, published in 2007 and updated in 2020^{24,25} and the Global Initiative for Asthma (GINA) Guidelines for the Management of Asthma and The GINA Guidelines for the Diagnosis and Treatment of Difficult-to Treat and Severe Asthma^{26,27} These guidelines are enhanced by a position paper on irritant asthma.²⁸

Diagnosing asthma in the WTC population

Asthma is defined as a heterogeneous disease with respiratory symptoms (wheeze, shortness of breath, chest tightness and cough) that vary over time and intensity, and variable expiratory airflow limitation. Environmental and occupational exposures, including those from irritants, are potential causes. Symptoms often predate an asthma diagnosis. Spirometry with assessment of bronchodilator reversibility is an initial step in an evaluation for asthma, however, bronchodilator reversibility may not always be detected, and spirometry may not fully characterize the respiratory symptoms. Bronchoprovocation, peak flow monitoring, clinical treatment trials, or exercise studies can also be considered. Fixed airflow obstruction consistent with chronic obstructive pulmonary disease may also occur in severe or longstanding asthma. Although not included in the guidelines referenced above, small airway abnormalities have been documented in symptomatic obstructive airway diseases using pathologic studies, imaging, and physiologic techniques, including respiratory oscillometry.^{29–31}

Asthma symptoms associated with WTC dust/fume exposure have been well-described in responder and pediatric and adult survivor populations. 9-20,32 Most have spirometry values within normal predicted values;11,12,33-36 airflow obstruction on spirometry is less common, but includes some who fit the definition of COPD.^{37–39} Because of symptoms consistent with asthma with normal spirometry, additional studies have been performed, which show bronchial hyperresponsiveness 10,12,20,34,40 and possible small airway

involvement. 35,41-44 Asthma presentation in WTC patients can be described as follows:

New onset WTC-related asthma

Many responders and survivors developed new asthma symptoms within days, months and years after their acute or chronic exposures to the WTC dust fumes. As such, most do not fit the definition of Reactive Airways Dysfunction (RADS), which requires acute onset of asthma.⁴⁵ The variable intensity of WTC exposure, the often delayed onset of symptoms, as well as the persistence of symptoms, is consistent with a diagnosis of "non-acute" irritant induced asthma (IIA).^{28,46-49}

WTC aggravated asthma

Some responders and survivors had preexisting asthma or childhood asthma with symptoms that worsened within a short period after their exposure to the WTC dust/fumes.

Asthma mechanisms and phenotypes

Asthma guidelines describe the presence of chronic airway inflammation^{26,50} and the phenotype has important implications for a personalized approach to management. Airway type 2 (T2) immune responses are mediated by eosinophils, mast cells, Th2 cells, group 2 innate lymphoid cells type 2, and/or IgE-producing B cells. Non-allergic stimuli (viruses, irritants, pollutants, tobacco smoke) can also activate T2 pathways. 50 In contrast, low T2 asthma is a diagnosis of exclusion, often associated with obesity/metabolic syndrome or environmental exposures.⁵¹ Fixed airflow obstruction consistent with COPD may occur with either.

Heterogeneity of WTC-related or aggravated asthma may be due to differences in WTC or other exposures (tobacco use, other occupations), social determinants of health, co-morbidities, as well as genetic underpinnings. Perennial and/or seasonal or mold allergen sensitization was noted in 17-40% of responders.^{37,52,53} Elevated levels of IL-5 and IL-4 are reported in firefighters, and blood neutrophil or eosinophil counts are associated with the decline or reduced FEV₁. 54,55 However, many WTCexposed patients with asthma symptoms have neither elevated total IgE, blood eosinophils nor FeNO. 37-39,54-56

Treatment of WTC-related or aggravated asthma

Current goals of asthma management are to reduce symptoms and minimize risk.²⁴⁻²⁷ Guidelines

reinforce the need to reduce modifiable risks such as tobacco use, and to use non-pharmacologic approaches (asthma education, trigger recognition and avoidance, pulmonary rehabilitation, weight management) and pharmacologic therapies with a patient-provider partnership. Assessment of symptom control including impairment (symptom frequency and functional status) and risk (exacerbations, reduced lung function) is stressed. Assessment of asthma severity is recommended only after treatment and incorporates the level of medication needed to control the disease. A written asthma action plan is also encouraged. Pharmacologic approaches include the early introduction of inhaled corticosteroids (ICS) either with a short acting β_2 agonist or as needed ICS-formoterol, even for mild asthma. Failing control, step-up therapy with an ICS and an inhaled long acting β_2 agonist, including single agent ICS-formoterol as maintenance and reliever therapy, and eventually anti-muscarinic agents are suggested.²⁶ Controlling co-morbidities including chronic rhinosinusitis with/without nasal polyposis, gastroesophageal reflux disease, elevated BMI, psychiatric disease, and metabolic syndrome is of great importance.²⁶ Patients with moderate-severe uncontrolled asthma who fail to attain control with these interventions should be referred to specialists for further diagnostic evaluation, phenotyping and consideration of add-on biologic agents targeting IgE, IL-5, IL-4Ra or thymic stromal lymphopoietin.²⁷

Few studies have examined pharmacologic efficacy in the WTC affected populations. One study suggests that early initiation of treatment is important for the reduction of long term effects.⁵⁷ A small study in survivors with persistent uncontrolled symptoms despite prescribed treatment, failed to show an improvement in symptom control despite adherence to high dose ICS-LABA.⁵⁸ Elevated BMI and metabolic syndrome are associated with persistence and worsening of symptoms, making these potential targets for treatment. 16-18,47,59-62

Program coverage

Asthma diagnostic services are covered by the WTC Health Program. For diagnostic coverage, the patient must be enrolled in the WTC Health Program. Treatment coverage requires that the enrolled member's asthma be certified. Asthma treatment is fully covered by the WTC Health Program for responders, and for survivors the treatment benefit is coordinated with other health insurance. To receive certification, a WTC Health Program-affiliated Clinical Center of Excellence (CCE) or the Nationwide Provider Network (NPN) must submit a WTC-3 form (https:// wws.cdc.gov/wtc/pdfs/Appendix-WTC3.pdf). other things, on the WTC-3 form, the CCE/NPN physician must attest that 9/11 exposures were substantially likely to have been a significant factor in aggravating, contributing to, or causing the enrolled WTC member's asthma. To receive asthma certification, the member must also satisfy 9/11 exposure (NIOSH 2015) and maximum time interval requirements (NIOSH 2017).

Conclusion

WTC-related or aggravated asthma is a common outcome of WTC exposures in responders and survivors. The disease is a heterogeneous disease with differing phenotypes and associated co-morbidities. These characteristics require personalized evaluation and approaches consistent with high quality asthma guidelines.

Disclosure statement

No potential conflict of interest was reported by the authors.

Disclaimer

The contents of this article are the sole responsibility of the authors and do not necessarily represent the official views of, nor an endorsement, by the National Institute for Occupational Safety and Health (NIOSH), the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services (CDC/HHS), or the U.S. Government.

Institutional review board (IRB) review

This activity did not involve human subjects and therefore did not require IRB review.

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