

# Occupational toxicant inhalation injury: the World Trade Center (WTC) experience

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## Abstract

**Objective and methods** Clinical descriptive data is presented on a group of 554 former workers and volunteers (with more than 90 different occupations) at the World Trade Center (WTC) disaster site. A subsample of 168 workers (30% of the group) was selected to examine lower airway disease risk in relation to smoking and WTC exposure variables.

**Results** Five diagnostic categories clearly predominate: upper airway disease (78.5%), gastroesophageal reflux disease (57.6%), lower airway disease (48.9%), psychological (41.9%) and chronic musculoskeletal illnesses (17.8%). The most frequent pattern of presentation was a combination of the first three of those categories (29.8%). Associations were found between arrival at the WTC site within the

first 48 h of the terrorist attack and lower airway and gastroesophageal reflux disease, and between past or present cigarette smoking and lower airway disease.

**Conclusion** Occupational exposures at the WTC remain consistently associated with a disease profile, which includes five major diagnostic categories. These conditions often coexist in different combinations, which (as expected) mutually enhances their clinical expression, complicates medical management, and slows recovery. Cigarette smoking and early arrival at the WTC site appear to be risk factors for lower airway disease diagnosis.

**Keywords** Occupational medicine · Inhalation injury · Asthma · Respiratory diseases · Irritant exposures

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## Introduction

The attack to the World Trade Center (WTC) in New York City on 11 September 2001, and the subsequent 9.5-month long massive effort to rescue, recover, and restore services to the area, exposed a large number of workers (unofficially estimated at about 40,000) to many occupational toxicants and stressors, which remain to be fully characterized. Although sampling and analysis of the WTC dust was delayed and limited, it is widely accepted that it was hazardous, containing a large amount of respirable particles, a high concentration of polyaromatic hydrocarbons, and, most notably, a very caustic pH (9.5–11) (Liroy et al. 2002). Other less well recognized occupational hazards included ergonomic (Berríos-Torres et al. 2003) and psychological stressors.

Early screening surveys of firefighters (Centers for Disease Control and Prevention 2002; Prezant et al. 2002), police officers (Salzman et al. 2004), and other workers (Levin et al. 2005) suggested a consistent pattern of

self-reported symptoms and spirometric abnormalities. Among the latter, a reduced forced vital capacity has been the most prevalent. Bronchial hyperreactivity has also been reported, and one of the surveys suggested early arrival at the WTC site (within the first 48 h of the attack) as a risk factor for it (Prezant et al. 2002). Importantly, symptom persistence has been suggested by a telephone survey study of police officers (Buyantseva et al. 2007). However, detailed clinical characterizations of those findings, as well as studies on additional occupational groups have not been published. The aim of this study was to describe the range of clinical characteristics of WTC-related diseases in a group of workers representative of the widest possible range of occupations deployed at the disaster site, and explore hazardous exposure risk factors for those conditions, particularly for lower respiratory disease.

## Methods

Patients were evaluated sequentially during the first year of operation of the World Trade Center Health Effects Treatment Program (WTC HETP) at Mount Sinai Medical Center in New York City. The WTC HETP (established in January of 2003) is dedicated exclusively to the diagnosis and treatment of adverse health effects observed in former rescue, recovery, and service restoration workers and volunteers at the WTC disaster site, the Staten Island landfill, and the barges that transported debris between those two sites. Eligibility to receive clinical services also required presence at the WTC site during the fall of 2001, as described elsewhere (Levin et al. 2005). Philanthropic funding allowed the WTC HETP to provide all diagnostic and treatment services to all segments of its patient population for the conditions reported herein. A total of 588 patients were evaluated during the first year of the program by three physicians (AAA, LAB, and RED), and reviewed prospectively and retrospectively by one of them (RED). The physicians' medical qualifications and clinical experience included occupational and environmental medicine (AAA and RED), internal medicine (LAB and RED), and pulmonary medicine (RED). The medical conditions of 34 patients were deemed unrelated to their WTC exposures or the clinical information was insufficient to formulate a firm diagnosis. This report will therefore, concern the remaining 554 workers. The Mount Sinai School of Medicine Institutional Review Board approved this review, exempting it from the requirement for informed consent.

Before presenting to the WTC HETP, all patients had already undergone basic testing at screening programs, or at the request of their primary care physicians. This basic testing consisted of blood tests (cell counts, chemistry and liver function panels), urine analysis, spirometry, and chest radiograph. Presence of potential WTC-related symptoms

and/or laboratory abnormalities prompted a referral to the WTC HETP for further clinical evaluation.

Diagnostic evaluation included a systematic standardized survey of symptoms, general and WTC-specific work exposure history, physical examination, pre- and post-bronchodilator spirometry, and further diagnostic tests as clinically indicated for each patient. Occupations were coded using the 1990 United States Census occupational codes. With more than 80% of the patients having at least one lower respiratory symptom, and cough being the most prevalent one, a previously published chronic cough clinical investigation algorithm was followed for all patients (Brightling et al. 1999). Accordingly, the most frequently performed diagnostic investigations included complete pulmonary function tests (pre- and post-bronchodilator spirometry, plethysmographic lung volume and diffusion capacity measurements) and/or methacholine bronchoprovocation (42%), ENT consultations with fiberoptic rhinolaryngoscopy (34%), psychiatric evaluations (41%), allergy testing (12.5%), upper digestive studies (9%), high-resolution chest CT scan (5%), and rehabilitation medicine evaluation (7%).

Physicians' diagnoses were based on clinical symptoms, physical findings, supportive diagnostic test data, and/or response to specific treatment. A diagnosis of upper airway disease (UAD) required the presence of at least three symptoms of rhinitis (Storaas et al. 2005), persistent for more than 8 weeks and unrelated to an infection, with or without associated symptoms of sinusitis, pharyngitis or laryngitis (clinical investigation algorithms are available from the authors). Pharyngolaryngoscopic findings were quantitatively assessed (Belafsky et al. 2001) by a single otolaryngologist (MRS). A diagnosis of lower airway disease (LAD) required the presence of symptoms of dyspnea associated with cough and/or wheezing, and the exclusion of infectious diseases. A diagnosis of gastroesophageal reflux disease (GERD) required the presence of heartburn with a frequency of at least once or twice weekly, and a response to a trial of proton pump inhibiting antacid (DeVault and Castell 1999). Mental health diagnoses (MHD) were confirmed and coded by psychiatrists or psychologists, according to the DSM-IV. WTC-relatedness was considered when the symptoms began while at the WTC site, or within 6 months of the last day worked, depending on the type of physical or mental health condition.

For pulmonary functional evaluation, all testing and interpretative approaches followed published American Thoracic Society recommendations, and confidence intervals were used to determine normality categorically for all pulmonary function measurements (American Thoracic Society 1991), using published prediction equations (Crapo et al. 1982; Hankinson et al. 1999; Miller et al. 1983). Complete pulmonary function testing (PFT) included pre- and post-bronchodilator spirometry, plethysmographic lung volume measurement, and diffusion capacity by the single-breath

method. A decreased FEV<sub>1</sub>/FVC ratio defined obstruction, an FEF<sub>50%</sub>/FIF<sub>50%</sub> > 1.0 defined inspiratory flow limitation, a decreased total lung capacity (TLC) defined restriction, an increased residual volume or TLC defined overinflation, and a 20% decrease in FEV<sub>1</sub> by a concentration of methacholine (PC<sub>20</sub>) not exceeding 10 mg/ml was considered evidence of significant bronchial hyperreactivity.

A sample of 168 patients (approximately 30% of the study population, hereafter designated “30% sample”) was randomly selected in order to assess associations between smoking and WTC dust exposures, with pulmonary function test results and lower airway disease diagnosis. The sampling process consisted of selecting every third or fourth of the sequentially ordered patient list. A patient was considered a lifetime nonsmoker if (s)he had smoked less than 20 packs of cigarettes (or 12 oz. of tobacco) in a lifetime, or less than 1 cigarette/day (or 1 cigar/week) for 1 year. A minimum of 12 months was required to deem a patient a former smoker (American Thoracic Society 1978). For analytical purposes, smokers were divided between ever smokers and lifetime

nonsmokers. Available WTC dust exposure indicators included the date of arrival at the WTC site on or after 11 September 2001, and duration of work at the WTC site. This subsample analysis allowed a further characterization of the type of lower airway disease previously diagnosed by clinicians. If bronchial hyperreactivity was absent, cases originally diagnosed by clinicians as irritant-induced asthma, were reclassified as chronic bronchitis when their chest CT scan was normal, or with small airway disease when their chest CT scan showed air trapping (Mendelson et al. 2007). Aggravated chronic lung diseases, usually smoking-related chronic obstructive pulmonary disease, was diagnosed when there was a history of tobacco smoking and decreased diffusion capacity in a previously asymptomatic person.

Statistical analyses were performed using SPSS software (SPSS Inc. 2003). The Chi square test and the Mann–Whitney tests were used to determine significant differences between two groups on categorical and continuous variables, respectively. Two-tailed statistical significance testing with a *P* level less than 0.05 was used throughout.

**Table 1** Patient characteristics

	<i>N</i> (%)
Male sex	422 (76.2%)
Age (years, mean ± SD)	44.8 ± 9.2
Non-English speakers	216 (39%)
Spanish speakers	170 (30.7%)
Polish speakers	44 (7.9%)
Major occupational groups	
Laborers (asbestos removers, building cleaners, construction and demolition laborers)	237 (42.8%)
Firefighters	69 (12.5%)
Construction trade workers (ironworkers, electricians, carpenters, plumbers)	63 (11.4%)
Police officers	33 (6%)
Health care workers (nurses, nurses' aides, emergency medical technicians)	9 (1.6%)

## Results

Table 1 summarizes the characteristics of the patient population. A large proportion of patients (37.9%) lacked any type of health insurance, and this was particularly pronounced for the Spanish speakers (75.2%). More than 90 occupations are represented. Most workers had several years of experience in their occupations, trade union membership was identified in 65.2% of the patients, and 7% of the workers volunteered their services at the site.

Five major disease categories have emerged in this patient population, as listed in Table 2. Those disease categories often coexist in different combinations. About three quarters of the patients (75.5%) presented with diagnoses in at least two of the five major categories, and close to half of them (48.2%) had diagnoses in at least three of those five categories. The large majority of patients with lower airway disease (91.1%) had a concomitant upper airway and/or

**Table 2** Most prevalent disease categories and diagnoses in 554 former WTC workers

Disease category	Most frequent diagnoses	%
Upper airway disorders (UAD)	Rhinitis, sinusitis, pharyngitis, laryngitis	78.5
Gastroesophageal reflux disease (GER)	Erosive and nonerosive, acid and nonacid reflux disease	57.6
Lower airway diseases (LAD)	Asthma and asthma variants, chronic bronchitis and bronchiolitis, aggravated pre-existing chronic obstructive lung disease	48.9
Mental health diseases (MHD)	Prolonged post-traumatic stress disorder, major depressive disorder, and agoraphobia with panic disorder	41.9
Musculoskeletal conditions (MSC)	Lumbar spine injuries (strain or sprain, with or without intervertebral disc disease), tendinitides	17.8

gastroesophageal reflux disease. In fact, the most frequent clinical presentation was a triad of upper and lower airway disease, and gastroesophageal reflux disease (29.8% of the patients, see Fig. 1).

Upper airway disease consisted most frequently of chronic perennial rhinitis, allergic or not, with associated sinusitis and/or pharyngitis in some cases. Five cases of vocal cord dysfunction were identified. GERD manifested with laryngopharyngeal symptoms and pharyngolaryngoscopic inflammatory findings (Belafsky et al. 2001) in virtually every patient given this diagnosis. Other extraesophageal manifestations of GERD were also frequent, including chronic cough and precordial noncardiac chest pain. Treatment frequently required double daily dosing of proton-pump inhibitor antacids for partial symptomatic control.

Lower airway disease usually consists of either irritant-induced asthma (with or without present evidence of bronchial hyperreactivity, 217/584, 37%), and aggravated chronic lung diseases, usually smoking-related chronic obstructive pulmonary disease (48/584, 8%). Further characterization of the suspected cases of asthma in the 30% sample indicated subsets of individuals who had a negative bronchoprovocation test, and thus could be reclassified as suffering from a chronic bronchitis picture (when their chest CT scan was normal) or with small airway disease (when their chest CT scan showed air trapping).

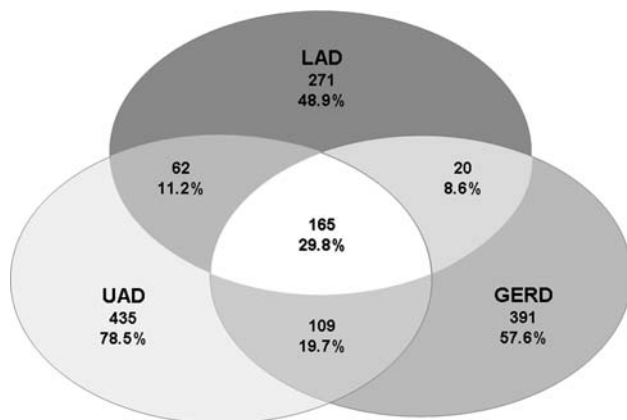
In the 30% sample, the proportions of lifetime nonsmokers, former and present smokers were, respectively, 48.2, 34.5, and 17.5%. Almost half of the patients (85/168, 50.6%) started working at the WTC site within the first 48 h of the terrorist attack. The mean exposure duration was 18.2 weeks (SD 15.6 weeks), and did not differ between those who arrived at the WTC site within the first 48 h or not ( $P = 0.25$ ). Table 3 summarizes the findings on pulmonary functional tests (168 spirometries, 62 plethysmographic lung volume and diffusion capacity tests, and 63 methacholine challenge tests). High-resolution chest CT

**Table 3** Pulmonary functional abnormalities in 168 patients (30% sample, 168 spirometries, and 62 complete PFTs)

Abnormalities	Frequency
Normal expiratory flows	102/168 (60.7%)
Reduced forced vital capacity	50/168 (29.8%)
With bronchodilator response	15/50
With concomitant obstruction	8/50
Bronchodilator response	35/168 (20.8%)
Inspiratory flow limitation	32/168 (18.6%)
Obstruction with normal FVC	20/168 (11.9%)
Restriction	16/62
Overinflation	12/62
Nonspecific bronchial hyperreactivity	17/63

scans ( $n = 28$ ) failed to reveal interstitial lung disease in any of the patients with restriction and/or decreased diffusion capacity. In patients with clinical diagnosis of irritant-induced asthma, bronchial hyperreactivity was not always evident or was mild (e.g.,  $PC_{20}$  of 8 or 10 mg/ml). In virtually all cases with bronchial hyperreactivity, the response pattern was characterized by a similar reduction in both FVC and  $FEV_1$  (Gibbons et al. 1996). This pattern was also the predominant one in those individuals (almost all of them firefighters) who had documented spirometric data from before 11 September 2001, and experienced excessive lung function decline, with subsequent complete, partial, or no recovery (data not presented).

Functional data in the 30% sample allowed further characterization of the cases of LAD (present in 90 of 168 patients), according to the subcategories described in “Methods”. The working diagnoses were irritant-induced occupational asthma, aggravated COPD, chronic bronchitis, and small airway disease in 38 (22.6%), 24 (14.3%), 22 (13.1%), and 6 (3.6%) of the patients, respectively.<sup>1</sup>



**Fig. 1** Co-existence of three major disease categories in former WTC workers ( $n = 554$ )

<sup>1</sup> Subsequent to the review and acceptance of this article, two patients suspected to have small airway disease (as described in “Methods” and “Results”), underwent thoracoscopic open lung biopsy, in view of their lack of adequate response to inhaled medications. The histology revealed constrictive bronchiolitis in one of the cases, which would lend support to the preliminary classification presented in this article. This patient (whose end-expiratory chest CT scan showed severe air trapping but no interstitial changes, and his pulmonary function tests borderline decreases in both total lung capacity and diffusion capacity) had, however, mild and patchy but definite focal lymphoid aggregates, areas of alveolar–capillary membrane thickening, and mild subpleural distal air space dilatation, but no honeycombing or fibroblastic foci. In the second case, the chest CT scan showed equally severe air trapping and interstitial changes, but the restriction and decreased diffusion were severe. The histologic features just described for the first case were similar but clearly more severe in the second case. Pending further characterization, the latter findings would add a new category of lung disease or broaden the spectrum or our understanding of the nature of the small airway disease category.

Lifetime nonsmokers were less likely to develop lower airway disease than ever smokers (37/81 or 45.7% vs. 53/87 or 60.9%, respectively,  $P = 0.048$ ). This difference was not observed for any of the other four disease categories. Ever smokers were more likely than lifetime nonsmokers to demonstrate obstruction in their spirometries (16/87 or 18.4% vs. 4/81 or 4.9%,  $P = 0.007$ ) but not FVC reduction (24/87 or 27.6% vs. 26/81 or 32.1%,  $P = 0.523$ ).

Workers who arrived at the WTC site within the first 48 h of the attack were more likely to develop lower airway disease and gastroesophageal reflux disease than those who arrived later (63/85 or 74.1% vs. 27/83 or 32.5%,  $P < 0.001$  for lower airway disease, and 66/85 or 77.6% vs. 48/83 or 57.8%,  $P = 0.006$  for gastroesophageal reflux disease). That association was not observed for the other three disease categories. Exposure duration, on the other hand, did not differ significantly between cases with and without any of the five major disease categories, or between those who arrived within or after the first 48 h of the terrorist attack (data not shown).

There does not seem to be any increased prevalence or consistent clinical patterns for other types of disease (e.g., dermatologic and neoplastic conditions). Five deaths have occurred within a 36-month follow-up. One death was due to end-stage coronary artery disease in a patient with severe WTC-related obstructive lung disease, and four to cancers. Of the cancers, one occurred in a patient who experienced a relapse of an ovarian cancer diagnosed and treated before 2001. The other three deaths resulted from tonsillar, brain, and kidney cancers, respectively.

## Discussion

Our data present a detailed clinical picture of the disease profile than has been suggested in previously published screening surveys (Buyantseva et al. 2007; Levin et al. 2005; Prezant et al. 2002; Smith et al. 2004), for the entire occupational range involved in the recovery of the WTC site, first evaluated and treated 16–28 months after the terrorist attack (or 6–18 months after the official end of the recovery of the WTC site).

Sampling and analysis of the WTC dust and other occupational hazards was delayed and limited. Dust collected after the collapse of the towers demonstrated a markedly alkaline pH (9.5–11.0 range), and excess content of polycyclic aromatic hydrocarbons (Lioy et al. 2002). The alkalinity of the dust is not surprising in view of its high cement content. Exposure to cement dust has been associated with adverse respiratory health effects (Al Neaimi et al. 2001; Mwaishelake et al. 2004). A very wide range of particle size was present, likely to affect every segment of the respiratory tract, from the nasal cavity to the bronchioles. Different

lines of evidence suggest that WTC dust induces self-perpetuating inflammatory and obstructive airway changes. WTC particulate matter induced cytokine release by primary human lung macrophage cell cultures (Payne et al. 2004), and bronchial hyperresponsiveness in exposed mice (Gavett et al. 2003). WTC dust exposure has been associated with prolonged airway inflammatory changes manifested in the induced sputum of New York firefighters (Fireman et al. 2004), and exposure intensity (particularly within the first 48 h of the towers collapse) has been associated with increased risk of spirometric abnormalities and persistent bronchial hyperreactivity (Banauch et al. 2003; Feldman et al. 2004; Prezant et al. 2002). Accordingly, our data suggest that early arrival at the WTC site was associated with more frequent diagnosis of chronic and persistent lower airway disease, and with reduced forced vital capacity by spirometry. These findings suggest that the characteristics of the dust (dose, particle size, and/or composition) varied along time. We also identified a history of cigarette smoking (present or previous) as an additional risk factor for the development of lower airway disease after occupational WTC exposures. Although exposure duration did not appear to be associated with being diagnosed with any of the five major disease categories, it can not be excluded as a risk factor for specific types of diseases.

Similarly to early screening survey reports, frequently encountered spirometric abnormalities in this population included a reduced forced vital capacity, and obstructive impairment. We found the former to be associated with early arrival to the WTC, but not with cigarette smoking. Besides asthma and aggravated COPD, small airway disease has been strongly suspected in many cases, but this diagnosis is difficult to make with conventional and/or available diagnostic tests. Several of our findings are either suggestive of or have been previously reported in small airway disease, including: (1) similarly reduced forced vital capacity and first-second forced vital capacity by spirometry (Guerry-Force et al. 1987), or upon methacholine bronchoprovocation (Gibbons et al. 1996); (2) restriction in the absence of interstitial, chest wall or neuromuscular causes, presumably due to loss of lung units in parallel distally to obstructed bronchioles (Guerry-Force et al. 1987); and (3) the frequent presence of concomitant obstructive or bronchoreactive features in our reduced FVC cases. Bronchiolitis obliterans has been already documented histologically in a former WTC worker (Mann et al. 2005). We are utilizing inspiratory and expiratory chest CT scans to investigate this type of condition, and report that separately (Mendelson et al. 2007).<sup>2</sup> The high prevalence of inspiratory flow limitation (suggestive of variable extrathoracic airway obstruction

<sup>2</sup> See footnote 1.

tion) probably contributes to explain some of the frequently reported respiratory symptoms. A small number of vocal cord dysfunction cases have been diagnosed so far (reported separately), and acid-reflux related laryngopharyngitis may also be another contributing factor. The prevalence of methacholine reactivity in our patients may have been reduced in part by the well-known time-related disappearance or attenuation of this abnormality in individuals diagnosed with occupational asthma (Malo and Ghezzeo 2004).

GERD is one of the most common and vexing clinical problems in WTC responders (prevalence close to 60% in our patient population). Virtually all patients presented with acid-reflux related laryngopharyngitis. There had been no clear precedent in other reported inhalation injury case series until the recent reports by Ghanei et al. (2005, 2006). GERD and airway and pulmonary disease (Ruigómez et al. 2005; Kempainen et al. 2007) have an unclear, probably bidirectional association, and it is notable that GERD and LAD were similarly associated with early arrival at the WTC site. Presently available data does not allow anything but speculations to explain the frequent finding of GERD in these patients. Toxicant inhalation may have triggered some upper digestive inflammation. But GERD may have also been pre-existent, perhaps subclinically (as it frequently can be) and then it may have been both (1) a predisposing factor for the post-exposure development of upper and perhaps also lower airway symptoms; and (2) a factor interfering with resolution of those symptoms despite exposure cessation (given its well known persistence and chronicity despite adequate treatment).

One of the most remarkable clinical findings in this population, in comparison to previous reports of toxicant inhalation injuries, is the high prevalence of comorbidity of lower airway disease with upper aerodigestive illness. There is little if any previously published finding of this nature. This may result from the increased awareness on the part of the medical community of the upper and lower airway disease connection, and of the complex relationship of GERD with lower airway disease (Kempainen et al. 2007; Ruigómez et al. 2005). Whatever the connection among these types of conditions, it is clear that clinical diagnosis and treatment are made more complex by their coexistence. Although causality can not be addressed by the data presented here, we believe that the experience with WTC-exposed workers is likely to change our understanding of toxicant inhalation injuries, and that the clinical model of the “chronic cough” clinics, similar to what we reported here, with a more comprehensive and multidisciplinary evaluation of the upper and lower respiratory, and upper digestive tract, will become the standard of care in future similar situations.

Several considerations deserve attention. One significant challenge in understanding the observed chronic disease profile is that although these conditions exhibit a high prevalence in our patient population, and there is for the most part considerable plausibility for their potential WTC-related occupational causation, many of the diseases are common in the general population at any given time. Studies comparing, within specific occupations, workers who did and did not participate in the WTC recovery effort are presently underway to answer this question. One such study has already documented an increased prevalence ratio for lower respiratory symptoms and illness in WTC exposed compared to unexposed firefighters (Feldman et al. 2004). Most of our workers had several years of experience in their occupations, and several but not all of the latter entail hazardous exposures that could result in some of the conditions reported here. It is quite remarkable, however, that the reported disease profile was so similar across occupational groups, although specific disease prevalence differences deserve further investigation in future studies. The major strength of this report is the presentation of individualized clinical data allowing the characterization of the diseases and syndromes identified in this patient population at this particular point in time. It is also strength of our study that the (philanthropic) funding of the HETP allowed it to investigate every patient diagnostically with identical level of detail. The clinical findings reported herein complement the survey (i.e., nondiagnostic) data already available in the literature. On the other hand, our patient population can not be expected to be a representative stratified sample of all the workers who participated in the WTC recovery duties, or even of those who report persistent symptoms. Whatever the true relative proportions, however, our patient population does include all the occupations present at the disaster site, and that constitutes another unique strength and contribution of this report.

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