FIRE DEPARTMENT

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Date: 9/3/2023

To: World Trade Center Health Program
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Administrator, World Trade Center (WTC) Health Program
and Director of the National Institute of Safety and Health (NIOSH)

CDR Brittany Rizek, M.P.H
Acting Division Administrative Director, WTC Health Program, NIOSH

Re: Petition to add rheumatologic systemic autoimmune diseases, even in the absence of pulmonary involvement, to the list of WTC-covered conditions under the Zadroga Act – including reference list with abstracts

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The Directors of the World Trade Clinical Centers of Excellence unanimously recommend to the WTC Health Program Administrator, that all rheumatologic systemic autoimmune diseases, regardless of whether pulmonary involvement exists, be added to the list of WTC-covered certifiable conditions under the Zadroga Act.

We petition the Administrator to add all rheumatologic systemic autoimmune diseases that are commonly grouped together to the list of WTC-covered conditions: Ankylosing Spondylitis, Anti-phospholipid Syndrome, Lupus, Myositis (Dermatomyositis, Polymyositis), Mixed or Undifferentiated Connective Tissue Disease, Psoriatic Arthritis, Rheumatoid Arthritis, Systemic Scleroderma, Sjögrens, Granulomatosis with Polyangiitis (previously called Wegner's granulomatosis), Eosinophillic Granulomatosis with Polyangiitis (previously called Churg-Straus) and Sarcoidosis. Please note we are <u>not</u> suggesting to add any of the non-rheumatologic diseases such as pernicious anemia or Hashimoto's thyroiditis.

We have reviewed the Administrator's recent published rule making policy for adding non-cancers as WTC-covered conditions. Our petition is based on evidence from four high-quality epidemiologic studies that demonstrate statistically significant associations between WTC exposure and new-onset rheumatologic systemic autoimmune disease in Responders and Survivors. Below, we summarize why we believe this evidence meets WTC Health Program

criteria for a "Category II (high likelihood for causal association)" designation and therefore qualifies for further review and a favorable decision.

Currently, rheumatologic systemic autoimmune disorders can only be certified as WTC-covered conditions if there is involvement of the pulmonary system (inflammation, fibrosis, nodularity, and/or intrathoracic adenopathy) after WTC exposure. WTC-certification has not been permissible if the rheumatologic systemic autoimmune disorder spared the pulmonary system and involved only joint, muscles, nerves, brain, heart, and/or other non-pulmonary organs.

A considerable amount of scientific, peer-reviewed, epidemiologic evidence has been published identifying that the most common rheumatologic systemic autoimmune diseases in WTC-exposed patients are in order of cumulative incidence – Sarcoidosis, Rheumatoid Arthritis, Lupus and Sjögren's (1,2,3,4). These studies add to what has already been well documented for Sarcoidosis (6-19).

Unlike other rheumatologic systemic autoimmune diseases, Sarcoidosis at diagnosis almost always includes the pulmonary system (6-19). Consequently, it is extremely rare for Sarcoidosis to not been certified as a WTC-covered condition. For that reason, the studies discussed, and the numbers cited (Table - page 6) in this petition do not include sarcoidosis even though it is a rheumatologic systemic autoimmune disease that should likewise be covered even in the absence of pulmonary system involvement.

Several years ago, the WTC Health Program Administrator denied a petition to add autoimmune diseases to the list of WTC-covered conditions. We believe that the primary rationale for this rejection was that the only cohort to have studied this was FDNY finding a conditional odds ratios for new-onset rheumatologic systemic autoimmune diseases to have increased by 13% (COR 1.13, 95% CI 1.02-1.26) for each additional month worked at the WTC site (1).

Confirmatory studies with the other WTC cohorts were encouraged by the WTC Health Program. It should also be noted that the original petition may have been interpreted as too broad a request - adding all autoimmune diseases rather than just rheumatologic systemic autoimmune diseases as we have specified in the current request. And, we have no intention of expanding this request.

Since that time, additional studies have been published by FDNY (2) and have been confirmed by the WTC Health Registry at the NYC Dept. of Health & Mental Hygiene (3,4), both of which demonstrated an association between WTC exposure and rheumatologic systemic autoimmune diseases after adjusting for age, sex, race and in one study also adjusting for PTSD (4). The FDNY study (2) found rates were not significantly different from expected rates (SIR, 0.97; 95% CI, 0.77-1.21), but an exposure gradient was identified with the lower WTC exposure group had 9.9 fewer cases than expected, whereas the higher WTC exposure group had 7.7 excess cases. In the WTC Registry study (3), responders with intense dust cloud exposure had almost twice the risk of rheumatologic systemic autoimmune diseases (adjusted risk ratio =1.86, 95% CI=1.02-3.40). Community members with PTSD had a nearly three-fold increased risk of rheumatologic systemic autoimmune diseases. A follow up study from the WTC Registry confirmed that responders with dust cloud exposure had almost twice the odds of rheumatologic systemic

autoimmune diseases, while among community members, those with 9/11-related PTSD had 2.5 times the odds of having rheumatologic systemic autoimmune diseases (95% CI: 1.39, 4.39).

Recently, a study from the General Responder Cohort (GRC) was published and failed to demonstrate an association with WTC exposure (5), although there was a signal for an increased cumulative incidence for new-onset Lupus. We acknowledge the considerable effort required for this study, and that its design was similar to studies performed by FDNY and the WTC Health Registry. But we feel it is important when considering this study to recognize its limitations. The GRC was unable to find medical records for324 persons (28%). And in contrast to FDNY and the WTC Health Registry, the GRC is an open enrollment cohort that has continued to except new enrollees even to this day – 22 years later. We understand the public health benefit of open enrollment, but use of such a cohort for epidemiologic research, particularly for determination of exposure-related incidence and prevalence rates, is always open to criticism and even more so for the WTC in that cohort enrollment confers substantial healthcare and financial benefits. These benefits include free annual medicals, free coverage of WTC-covered conditions and easier access to lucrative financial compensation payments from the Victims Compensation fund, some of which existed within a year or two after the disaster and expanded further with the enactment of the WTC Zadroga Bill in 2010.

This can bias health surveillance findings in both positive and negative ways. For illnesses such as cancers that are widely known to be covered by the program and subject to healthcare/financial benefits, it can lead to preferential enrollment, falsely increasing incidence/prevalence rates. For autoimmune diseases not covered by the program and therefore not subject to healthcare/financial benefits, it disincentivizes enrollment, leading to under enrollment and the potential for falsely low incidence/prevalence rates. And, such loosely constructed cohorts, are often subject to longitudinal dropout and under-reporting of non-covered conditions due to perceived lack of interest or benefit for non-covered conditions such as autoimmune diseases. Finally, autoimmune diseases are multi-system diseases that often present with vague constitutional symptoms (intermittent fevers, fatigue, rashes, weight loss, joint stiffness/pain, palpitations, dizziness, etc.). Due to WTC Health Program regulations, there is no ability to use program funds to diagnose autoimmune diseases when such symptoms do not suggest a covered condition or there are no suspicions/findings of pulmonary involvement.

An example of under-reporting is the recent study from a single, specialty hospital, NOT a WTC Health Program Clinical Center of Excellence, identifying 11 cases of systemic sclerosis (submitted for publication - JM). From the case histories present in this study, many of the 11 patients were WTC-exposed and were or could be enrolled in a GRC or Survivor CCE. This case series highlights that individuals with WTC exposures seek care for auto-immune conditions outside the WTC Health Program, which may lead to an under counting of the true effect of 9/11 on exposed persons.

The WTC Survivor Program, a separate cohort, is unable to provide incidence or prevalence data because by legislation its cohort construction is only allowed to enroll symptomatic persons. However, the WTC Health Registry did find an association between WTC exposure and rheumatologic systemic autoimmune diseases in a separate analysis of community members other than responders (3,4).

In contrast to the GRC and the Survivor Program, the FDNY cohort and the WTC Health Registry are closed cohorts. The FDNY cohort meets the highest level of certainty in that all members were enrolled in FDNY's health surveillance/maintenance system prior to 9/11 and exposure is the most easily verified. It is a relatively homogeneous cohort with pre-9/11 health data. The cohort has excellent health insurance independent of the Zadroga Act and therefore is not limited to diagnostic studies covered by the WTC Health Program, thereby allowing for diagnosis of these rheumatologic systemic autoimmune diseases. The DOHMH WTC Health Registry is nearly as purely designed in that enrollment ended in 2003 prior to the widespread availability of the above noted WTC-related benefits (healthcare and financial). Compared to FDNY, the WTC Health Registry cohort is a more heterogeneous group of responders, workers, residents with variable exposures and variable access to health insurance coverage.

Based on confirmatory evidence from these cohorts (The WTC Health Registry including both responders and community members) and limitations to the one cohort that failed to find confirmation, we believe the WTC Health Program Administrator, should reconsider the initial, now out-of-date, decision and add all rheumatologic systemic autoimmune diseases with new-onset after WTC exposures to the list of WTC-covered conditions, regardless of whether pulmonary involvement exists.

We have reviewed the Administrator's published rule making decision for covering cancers and the recent published rule making process to add non-cancers as WTC-covered conditions. We believe that covering rheumatologic systemic autoimmune diseases is consistent with the same method / logic outlined in both documents. In fact, we believe the evidence is even stronger than that originally provided to include many of the cancers currently on the WTC-covered condition list.

Our petition is based on evidence from four of five studies that demonstrate a statistically significant association between WTC exposure and new-onset rheumatologic systemic autoimmune disease in Responders and Survivors. Based on this evidence we believe our petition deserves at least a Category II designation.

According to the WTC Health Program's Policy for adding non-cancer health conditions to the list of WTC-related health conditions, petitions based on Category II evidence allow the Administrator to consider additional data from the following sources:

1. Sources of highly relevant scientific information regarding non-9/11 exposures published (or funded) by the US government, including the National Toxicology Program (NTP)
2. Evaluation of additional highly relevant scientific information regarding non-9.11 exposures – bioplausibility based on physical and mental health exposures
3. Findings and recommendations solicited from the WTC Clinical Centers of Excellence and Data Centers, and the WTC Health Registry at the New York City Department of Health and Mental Hygiene
4. Findings and recommendations from other sources of information relevant to 9/11 exposures, including expert judgment from the NIOSH WTC Science Team and the NIOSH WTC Scientific Advisory Committee (STAC)

5. Information from the public solicited through a request for information published in the *Federal Register*

Using the same considerations as the WTC Health Program Administrator used for decisions to include cancers as WTC-covered conditions, our rationale for a favorable decision on our petition uses evidence from each of the five additional sources as follows:

1. The National Toxicology Program (NTP) is an interagency program in NIEHS tasked with evaluating agents of public health concern using toxicology and molecular biology. NTP findings were used by the Administrator in his explanation for covering cancers, even those without epidemiologic evidence in WTC cohorts, under the Zadroga Act. The NTP studies more than just cancer – it also evaluates the impact of toxic exposures on autoimmune diseases. In 2012 and 2014, the NTP published an expert panel workshop consensus statement on the role of the environment in the development of autoimmune diseases (20-22).

   The expert panel reported with "confidence" that:
   - Crystalline silica (quartz) contributes to development of several rheumatologic systemic autoimmune diseases, including rheumatoid arthritis, systemic sclerosis, systemic lupus erythematous, and anti-neutrophil cytoplasmic antibody (ANCA)-related vasculitis.
   - Solvents contribute to development systemic sclerosis.
   - Smoking contributes to development of anti-citrullinated protein antibody (ACPA)-positive and anti-rheumatoid factor - positive rheumatoid arthritis (with an interaction with the shared genetic susceptibility factor).

   Note that "a confident" association was defined by the NTP as evidence from multiple studies in different populations using different designs; robust evidence of an overall association (*i.e.*, high magnitude risks or based on high quality or established exposure assessment methods); a dose-response relationship, or effect differences by disease subtype or genetic factors supporting biologic plausibility.

2. Additional highly relevant scientific information regarding non-9/11 exposures.

   A. Bioplausibility based on physical exposures exists for associations between WTC exposures (23) and rheumatologic autoimmune disease. Crystalline silica, a risk factor for rheumatologic systemic autoimmune diseases (24-31) was a major component of the dust cloud (23). Additional components of the toxic dust and air at the site during the clean-up period (20,23) have been previously associated with rheumatologic systemic autoimmune diseases, including asbestos (32, 33), organic hydrocarbon solvents (29, 34-36), diesel fuel (37) and fine particulate matter [PM2.5] (38-41).

   B. Bioplausibility based on mental health exposures: many people witnessed traumatic events on 9/11 as well as continued personal reminders of the attack. The association between rheumatologic systemic autoimmune diseases and posttraumatic stress disorder (PTSD) has been demonstrated in both veterans and civilian populations (42,43,44) and

has now been demonstrated by the WTC Registry in WTC-exposed community members suffering from WTC-related PTSD (4).

3. Findings and recommendations from WTC Clinical Centers of Excellence Program Directors: based on published peer-reviewed papers (1-5) and annual reports, the WTC Health Program has approximately ~550 patients with confirmed rheumatologic systemic autoimmune diseases (other than pulmonary sarcoidosis) whose WTC-certification requests would be affected by this regulatory change (see table below). This is an underestimate as this data is not currently available from the Survivor Program and has not been recently updated by the other programs. Regardless, the existing data indicates that rheumatologic systemic autoimmune diseases are relatively rare compared to other covered conditions in the WTC Health Program. While extending WTC coverage to include these diseases should have minimal impact on the Program, it will have significant impact on affected members. For these reasons, we are unanimous in our request that ALL rheumatologic systemic autoimmune diseases conditions be added to the list of WTC-covered conditions.

Rheumatologic Systemic Autoimmune Diseases*	FDNY[a]	General Responders[b]	WTC Registry[c]
Rheumatoid Arthritis	49	110	71
Psoriatic Arthritis	30	44	
Poly/Dermatomyositis	10	<10	9
Scleroderma	5	10	4
Systemic Lupus Erythromatosis (SLE)	14	26	20
Sjögrens	4	12	22
Antiphospholipid Syndrome	5	<10	
Granulomatosis with polyangiitis (previously called Wegner's granulomatosis),	2	16	
Other (Ankylosing Spondylitis, and Eosinophillic Granulomatosis with polyangiitis (previously called Churg-Straus)	5	22	
Mixed Connective Tissue Diseases		25	7
Total diagnoses (some patients have >1)	125	274	133
a = new onset 2002 to 2022 *b = new onset 2002 through 2017* *c = new onset 2002 through 2017* **Note: data is not available from the Survivor Cohort, but survivors (community residents, etc.) are included in the WTC Registry*			

4. Findings, recommendations and expert judgment from others including the NIOSH WTC Science Team and the NIOSH WTC Scientific Advisory Committee (STAC): given that the statistical evidence for an association between WTC exposure and new-onset rheumatologic systemic autoimmune diseases is as strong if not stronger than it was for many of the WTC-covered cancers, we are confident that that our petition will receive serious consideration and ultimately their support.

5. We are very confident that public comment will be favorable. The science, the impact these conditions have on quality of life, and the availability of FDA-approved treatments that unquestionably improve quality of life and prognosis, should provide the basis for such support.

Several important additional points are supported by the rheumatologic literature and argue for covering ALL rheumatologic systemic autoimmune diseases as WTC-covered conditions.

First, it is well known that in the general population (non-WTC-exposed), rheumatologic systemic autoimmune diseases occur more often in females. This makes it even more remarkable that in predominantly male WTC cohorts an increased incidence of rheumatologic systemic autoimmune diseases was found.

Second, for any individual patient over time there is significant overlap and movement from one rheumatologic disease to another. Many patients will initially be diagnosed with one condition and then overtime have their diagnosis changed to another rheumatologic systemic autoimmune disease (45-47). At presentation approximately a quarter to one-third of connective tissue diseases are "overlap, mixed or undifferentiated." As many as 28% of patients initially given the diagnosis of "undifferentiated connective tissue disease" will within 5 to 7 years evolve into another well-defined rheumatologic systemic autoimmune disease, most often, rheumatoid arthritis and lupus (48). In one study of 100 patients over several years, it was determined that such patients eventually met criteria for systemic scleroderma, polymyositis/dermatomyositis or rheumatoid arthritis. New clinical manifestations were seen in 39 patients during the 6 years of follow up and included hematologic (30%), pulmonary (10%) and renal (10%) involvement (49). And, in the previously mentioned case series of 11 WTC-exposed patients with systemic scleroderma patients, 45 met diagnostic criteria for an overlapping rheumatologic systemic autoimmune disease (submitted for publication - JM). Rheumatologists recognize that many patients do not initially fulfill criteria for a specific systemic rheumatologic autoimmune disease, but eventually will, and therefore still require monitoring and treatment to improve long term patient outcomes by preventing disease progression and the appearance of new potentially irreversible manifestations.

Third, the current WTC-certification requirement that the pulmonary involvement must be evident is contrary to well-established science that rheumatologic systemic autoimmune diseases are multi-organ, systemic diseases that affect any organ and that the organ(s) involved may change over time. The absence of pulmonary involvement for sarcoidosis or for any rheumatologic systemic autoimmune disease does not preclude that WTC exposure (respirable, gastroesophageal, or dermal) triggered a systemic

inflammatory response affecting any organ system. The lungs through their robust immunologic response and extensive alveolar-capillary-lymphatic circulation are but one window providing access to the whole body. Inflammation is a systemic process. In the FDNY sarcoid study (6) pulmonary involvement was present initially, but over time resolved in ~45% while involvement of other organs, notably joint and cardiac, occurred years later. If these patients were not found through annual monitoring and presented instead at a later time, the pulmonary involvement would have been missed. Their WTC-certification request would have stated an absence of pulmonary involvement even though that was not originally the case, and their WTC-certification request would have been unfairly denied. For systemic rheumatologic systemic autoimmune diseases other than sarcoidosis, the opposite may occur – initial presentation that does not involve pulmonary manifestations, which then develop at a later time. For rheumatoid arthritis, disease severity and longer duration have been shown to be associated with higher likelihood of developing interstitial lung disease at a later time (50). Six months after diagnosis, the presence of at least one pulmonary item in the Vasculitis Damage Index was observed in 15% of patients with Granulomatosis with polyangiitis (previously called Wegner's Granulomatosis), and in 53% of patients with Eosinophillic Granulomatosis with polyangiitis (previously called Churg Strauss Disease) (51). In the previously mentioned case series of 11 WTC-exposed patients with systemic scleroderma patients, 91% eventually developed interstitial lung disease (submitted for publication - JM). These studies demonstrate that withholding WTC-certification for rheumatologic systemic autoimmune diseases due to the absence of pulmonary disease at any moment in time ignores the evidence that progression to other organs is common and denies patients an opportunity for early treatment that can halt or reduce progression.

In summary, the WTC Health Program Directors from all of the WTC Clinical Centers of Excellence (FDNY, Mount Sinai. Stony Brook, Northwell, NYU, Robert Wood Johnson and the Survivor Program at Bellevue) unanimously and respectfully request that the WTC Administrator allow the NIOSH WTC Health Program Science Team and the STAC to review whether WTC Health Program coverage can be extended to all rheumatologic systemic autoimmune diseases presenting without pulmonary involvement. This would include adding the following diseases to the list of WTC-covered conditions: Ankylosing Spondylitis, Anti-phospholipid Syndrome, Lupus, Myositis (Dermatomyositis, Polymyositis), Mixed or Undifferentiated Connective Tissue Disease, Psoriatic Arthritis, Rheumatoid Arthritis, Sarcoidosis, Systemic Scleroderma, Sjögrens, Granulomatosis with polyangiitis, and Eosinophillic Granulomatosis with polyangiitis. To maintain the program's credibility and its fiduciary responsibility, we recommend that such coverage require the same exposure requirements as required for WTC cancers – new onset occurring post-9/11 and only in those with significant WTC exposure.

Respectfully,

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Attached: Reference list with relevant abstracts

References:

A. Rheumatologic Systemic Autoimmune Diseases Other Than Sarcoidosis:

1. Webber MP, Moir W, Zeig-Owens R, Glaser MS, Jaber N, Hall C, Berman J, Qayyum B, Loupasakis K, Kelly K, Prezant DJ. Nested case-control study of selected systemic autoimmune diseases in World Trade Center rescue/recovery workers. Arthritis Rheumatol. 2015 May;67(5):1369-76. doi: 10.1002/art.39059. PMID: 25779102

Abstract
OBJECTIVE: To test the a priori hypothesis that acute and chronic work exposures to the World Trade Center (WTC) site on or after September 11, 2001, were associated with risk of new-onset systemic autoimmune diseases.
METHODS: A nested case-control study was performed in WTC rescue/recovery workers who had received a rheumatologist-confirmed systemic autoimmune disease diagnosis between September 12, 2001, and September 11, 2013 (n = 59), each of whom was individually matched to 4 randomly selected controls (n = 236) on the basis of year of hire (±1 year), sex, race, and work assignment (firefighter or emergency medical service). Acute exposure was defined according to the earliest time of arrival (morning of 9/11 versus later) at the WTC site, and chronic exposure was defined as duration (number of months) of WTC site-related work. Rheumatologists were blinded with regard to each subject's exposure status. The conditional odds ratios (CORs) with 95% confidence intervals (95% CIs) for incident autoimmune disease were derived from exact conditional logistic regression models.
RESULTS: Rheumatoid arthritis was the most common autoimmune diagnosis (37% of subjects), followed by spondyloarthritis (22%), inflammatory myositis (14%), systemic lupus erythematosus (12%), systemic sclerosis (5%), Sjögren's syndrome (5%), antiphospholipid syndrome (3%), and granulomatosis with polyangiitis (Wegener's) (2%). The COR for incident autoimmune disease increased by 13% (COR 1.13, 95% CI 1.02-1.26) for each additional month worked at the WTC site. These odds were independent of the association between high acute exposure (working during the morning of 9/11) and disease outcome, which conveyed elevated, but not statistically significant, risk (COR 1.85, 95% CI 0.86-3.89).
CONCLUSIONS: Prolonged work at the WTC site, independent of acute exposure, was an important predictor of post-9/11 systemic autoimmune diseases. The WTC Health Program should expand surveillance efforts for those with extended exposures, as early detection can facilitate early treatment, which has been shown to minimize organ damage and improve quality of life.

2. Webber MP, Moir W, Crowson CS, Cohen HW, Zeig-Owens R, Hall CB, Berman J, Qayyum B, Jaber N, Matteson EL, Liu Y, Kelly K, Prezant DJ. Post-September 11, 2001, Incidence of Systemic Autoimmune Diseases in World Trade Center-Exposed Firefighters and Emergency Medical Service Workers. Mayo Clin Proc. 2016 Jan;91(1):23-32. doi: 10.1016/j.mayocp.2015.09.019. Epub 2015 Dec 9. PMID: 26682920

Abstract
OBJECTIVE: To estimate the incidence of selected systemic autoimmune diseases (SAIDs) in approximately 14,000 male rescue/recovery workers enrolled in the Fire Department of the City of New York (FDNY) World Trade Center (WTC) Health Program and to compare FDNY incidence to rates from demographically similar men in the Rochester Epidemiology Project (REP), a population-based database in Olmsted County, Minnesota.
PATIENTS AND METHODS: We calculated incidence for specific SAIDs (rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, and others) and combined SAIDs diagnosed from September 12, 2001, through September 11, 2014, and generated expected sex- and age-specific rates based on REP rates. Rates were stratified by level of WTC exposure (higher vs lower). Standardized incidence ratios (SIRs), which are the ratios of the observed number of cases in the FDNY group to the expected number of cases based on REP rates, and 95% CIs were calculated.

RESULTS: We identified 97 SAID cases. Overall, FDNY rates were not significantly different from expected rates (SIR, 0.97; 95% CI, 0.77-1.21). However, the lower WTC exposure group had 9.9 fewer cases than expected, whereas the higher WTC exposure group had 7.7 excess cases. CONCLUSIONS: Most studies indicate that the healthy worker effect reduces the association between exposure and outcome by about 20%, which we observed in the lower WTC exposure group. Overall rates masked differences in incidence by level of WTC exposure, especially because the higher WTC exposure group was relatively small. Continued surveillance for early detection of SAIDs in high WTC exposure populations is required to identify and treat exposure-related adverse effects.

3. Miller-Archie SA, Izmirly PM, Berman JR, Brite J, Walker DJ, Dasilva RC, Petrsoric LJ, Cone JE. Systemic autoimmune disease among adults exposed to the September 11, 2001, terrorist attack. Arthritis Rheumatol. 2019 Nov 24. doi: 10.1002/art.41175. [Epub ahead of print]. PMID: 31762219

Abstract
OBJECTIVE: Autoimmune disease is an emerging condition among persons exposed to the September 11, 2001, attack on the World Trade Center (WTC). Components of the dust cloud resulting from the collapse of the WTC have been associated with systemic autoimmune diseases (SAID), as has posttraumatic stress disorder (PTSD). We sought to determine whether dust exposure and PTSD were associated with an increased risk of SAID in a 9/11-exposed cohort.
METHODS: Among 43,133 WTC Health Registry enrollees, 2,786 self-reported a post-9/11 SAID. We obtained consent to review medical records to validate SAID diagnoses for 1,041. SAIDs were confirmed by classification criteria, rheumatologist diagnosis, or having been prescribed SAID medication. Controls were enrollees who denied an autoimmune disease diagnosis (n=37,017). We used multivariable log-binomial regression to examine the association between multiple 9/11 exposures and risk of post-9/11 SAID, stratifying by responders and community members.
RESULTS: We identified 118 persons with SAID. Rheumatoid arthritis was most frequent (n=71), followed by Sjögren's syndrome (n=22), systemic lupus erythematosus (n=20), myositis (n=9), mixed connective tissue disease (n=7), and scleroderma (n=4). Among 9/11 responders, those with intense dust cloud exposure had almost twice the risk of SAID (adjusted risk ratio =1.86, 95% CI=1.02-3.40). Community members with PTSD had a nearly three-fold increased risk of SAID.
CONCLUSIONS: Intense dust cloud exposure among responders and PTSD among community members were associated with a statistically significant increased risk of new-onset SAID. Clinicians treating 9/11 survivors should be aware of the potential increased risk of SAID in this population.

4. Brite J, Miller-Archie SA, Cone J.
The Relationship between 9/11 Exposure, Systemic Autoimmune Disease, and Post-Traumatic Stress Disorder: A Mediational Analysis. Int J Environ Res Public Health. 2022 May 27;19(11):6514. doi: 10.3390/ijerph19116514.

Abstract
The relationship between 9/11 exposure, systemic autoimmune disease (SAD) and mental health remains poorly understood. This report builds on a prior analysis of World Trade Center Health Registry data to determine whether 9/11 exposure is associated with higher risk of SAD, and if so, whether post-traumatic stress disorder (PTSD) is a mediating factor and whether the association varies by responder/community member status. The final analytic sample comprised 41,656 enrollees with 123 cases of SAD diagnosed post 9/11 through November 2017. SAD diagnosis was ascertained from survey responses and confirmed by medical record review or physician survey. Logistic regression models were constructed to determine the relationship between 9/11 exposure and PTSD and SAD. Causal mediation analysis was used to determine the mediational effect of PTSD. Each analysis was stratified by 9/11 responder/community member status. Rheumatoid arthritis (n = 75) was the most frequent SAD, followed by Sjögren's syndrome (n = 23), systemic lupus erythematosus (n = 20), myositis (n = 9), mixed connective tissue disease (n =

7), and scleroderma (n = 4). In the pooled cohort, those with 9/11-related PTSD had 1.85 times the odds (95% CI: 1.21-2.78) of SAD. Among responders, those with dust cloud exposure had almost twice the odds of SAD, while among community members, those with 9/11-related PTSD had 2.5 times the odds of SAD (95% CI: 1.39, 4.39). PTSD was not a significant mediator. Although emerging evidence suggests 9/11 exposure may be associated with SAD, more research is needed, particularly using pooled data sources from other 9/11-exposed cohorts, to fully characterize this relationship.

5. Sacks HS, Smirnoff M, Carson D, Cooney ML, Shapiro MZ, Hahn CJ, Dasaro CR, Crowson C, Tassiulas I, Hirten RP, Cohen BL, Haber RS, Davies TF, Simpson DM, Crane MA, Harrison DJ, Luft BJ, Moline JM, Udasin IG, Todd AC, Sloan NL, Teitelbaum SL. Autoimmune conditions in the World Trade Center general responder cohort: A nested case-control and standardized incidence ratio analysis. Am J Ind Med. 2022 Feb;65(2):117-131. doi: 10.1002/ajim.23313. Epub 2021 Nov 25.

Abstract
BACKGROUND: The World Trade Center (WTC) general responder cohort (GRC) was exposed to environmental toxins possibly associated with increased risk of developing autoimmune conditions.
OBJECTIVES: Two study designs were used to assess incidence and risks of autoimmune conditions in GRC.
METHODS: Three clinically trained professionals established the status of possible GRC cases of autoimmune disorders adhering to diagnostic criteria, supplemented, as needed, by specialists' review of consenting responders' medical records. Nested case-control analyses using conditional logistic regression estimated the risk associated with high WTC exposure (being in the 9/11/2001 dust cloud or ≥median days' response worked) compared with low WTC exposure (all other GRC members'). Four controls were matched to each case on age at case diagnosis (±2 years), sex, race/ethnicity, and year of program enrollment. Sex-specific and sensitivity analyses were performed. GRC age- and sex-adjusted standardized incidence ratios (SIRs) were compared with the Rochester Epidemiology Project (REP). Complete REP inpatient and outpatient medical records were reviewed by specialists. Conditions meeting standardized criteria on ≥2 visits were classified as REP confirmed cases.
RESULTS: Six hundred and twenty-eight responders were diagnosed with autoimmune conditions between 2002 and 2017. In the nested case-control analyses, high WTC exposure was not associated with autoimmune domains and conditions (rheumatologic domain odds ratio [OR] = 1.03, 95% confidence interval [CI] = 0.77, 1.37; rheumatoid arthritis OR = 1.12, 95% CI = 0.70, 1.77). GRC members had lower SIR than REP. Women's risks were generally greater than men's.
CONCLUSIONS: The study found no statistically significant increased risk of autoimmune conditions with WTC exposures.

B. Extrathoracic Sarcoidosis

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