

**Post-9/11 Incidence of Systematic Autoimmune Diseases in the FDNY
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Post-9/11 Incidence of Systemic Autoimmune Diseases in the FDNY Cohort

The overall goal of this two-year project was to calculate the incidence of selected systemic autoimmune diseases (SAID) in 21,786 World Trade Center (WTC)-exposed and unexposed firefighters and emergency medical service (EMS) workers and to estimate the association between intense WTC exposure and SAID. This proposal originated from the World Trade Center Health Program at the Fire Department of New York City (FDNY) where investigators have full access to FDNY monitoring and treatment records, excellent cohort retention rates, demonstrated ability to contact members for additional information, as required, and accurate estimates of person-time at risk from employment records. The following SAID diagnoses were included: systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), systemic sclerosis (SSc, including diffuse or limited), inflammatory myositis (dermatomyositis, polymyositis, or inclusion-body myositis), Sjögren's syndrome, rheumatoid arthritis (RA), and inflammatory arthritis (i.e., psoriatic arthritis and spondyloarthritis).

There had been no epidemiologic studies of SAID incidence or prevalence in WTC-exposed cohorts. WTC-related SAID arose as a concern because previous studies of non-WTC exposed workers demonstrated increased risk of SAID including SLE, SSc and RA, after exposure to agents such as silica, which was known to be present at the WTC disaster site.

The specific aims of this proposal were to:

Aim 1: Estimate the incidence of confirmed cases of SAID in the FDNY population (firefighters and EMS workers) from 9/11/2001 until 9/10/2013.

Aim 2: Perform a nested case-control study to estimate the effect size of WTC exposure on confirmed cases of all subtypes of SAID combined.

This cooperative agreement has yielded three peer-reviewed publications and one published letter, to date.

Original Aim 1: Estimate the incidence of cases of systemic autoimmune diseases (SAID) in the FDNY population (firefighters and EMS workers) from 9/11/2001 until 9/10/2013.

We completed work on this aim, culminating in an article in *Mayo Clinic Proceedings* (1).

Major findings:

- We included the following rheumatologist-confirmed diagnoses in our definition of SAIDS: rheumatoid arthritis, spondyloarthritis, inflammatory myositis, systemic lupus erythematosus, systemic sclerosis, Sjögrens syndrome, antiphospholipid syndrome and granulomatosis with polyangiitis (Wegener's).
- Using a sensitive definition of SAIDS, we identified 97 cases in the FDNY cohort of ~14,000 male rescue/recovery workers enrolled in The Fire Department of the City of New York (FDNY) World Trade Center (WTC) Health Program.
- Overall, FDNY SAIDs rates were **not** significantly different from expected rates as projected using age-and sex-specific rates from demographically similar men in the Rochester Epidemiology Project (REP), a population-based database in Olmsted County, MN.
- When FDNY rates were stratified by low versus high level of WTC exposure, the lower-WTC-exposure group had 10 *fewer* cases than expected, which we attribute to the healthy worker effect, whereas the higher-WTC-exposure group had 7.7 *excess* cases, which we attribute to WTC exposure.
- In conclusion, overall SAIDs rates masked differences in incidence by level of WTC exposure, especially as the higher-WTC-exposure group was relatively small.
- Continued surveillance for early detection of SAIDs in highly-WTC-exposed populations is required to identify and treat exposure-related adverse effects.

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.

CONCLUSION:

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.

Original Aim 2: Perform a nested case-control study to estimate the effect size of WTC exposure on confirmed cases of all subtypes of SAID combined.

We completed work on this aim, culminating in an article and a response letter to the editor in *Arthritis and Rheumatism* (2,3).

Major findings:

- Rheumatoid arthritis (37%) was the most common SAIDs diagnosis, followed by spondyloarthritis (22%), inflammatory myositis (14%), systemic lupus erythematosus (12%), systemic sclerosis (5%), Sjögrens syndrome (5%), antiphospholipid syndrome (3%) and granulomatosis with polyangiitis (Wegener's) (2%).
- The conditional odds ratio (COR) of autoimmune disease increased by 13% for each additional month worked at the WTC site (95% CI 1.02-1.26) and was independent of the association between high acute exposure (working during the morning of 9/11/2001) and disease outcome, which was elevated, but not statistically significant (COR 1.85 95% CI 0.86-3.89).
- Prolonged work at the WTC site, independent of acute exposure, was an important predictor of post-9/11 systemic autoimmune diseases in the FDNY cohort.
- The World Trade Center 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.

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 an elevated, but not statistically significant, risk (COR 1.85, 95% CI 0.86-3.89).

CONCLUSION:

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.

Because our clinical colleagues identified an unusual treatment response in persons with post-9/11 sarcoid arthritis, we published a case series describing this group in the *Journal of Clinical Rheumatology* (4).

Major findings:

- The objective of this study was to describe cases of sarcoid arthritis in firefighters from the Fire Department of the City of New York (FDNY) who worked at the World Trade Center (WTC) site.
- Diagnoses were based on clinical, radiographic, and pathological criteria. Patient characteristics, WTC exposure information, smoking status, date of diagnosis, and pulmonary findings were obtained from the FDNY-WTC database. Joint manifestations (symptoms and duration, distribution of joints involved), radiographic findings, and treatment responses were obtained from chart reviews.
- Nine of 60 FDNY firefighters who developed sarcoidosis since 9/11/2001 presented with polyarticular arthritis. Two others diagnosed pre-9/11/2001 developed sarcoid arthritis after WTC exposure.
- All 11 never smoked cigarettes, and all performed rescue/recovery at the WTC site within 3 days of the 9/11 attacks. All had biopsy-proven pulmonary sarcoidosis, and all required disease-modifying antirheumatic drugs for adequate control (stepwise progression from hydroxychloroquine to methotrexate to anti-tumor necrosis factor α agents) of their joint manifestations.
- Chronic inflammatory polyarthritis appears to be an important manifestation of sarcoidosis in FDNY firefighters with sarcoidosis and WTC exposure.
- Their arthritis is chronic and, unlike arthritis in non-WTC-exposed sarcoid patients, inadequately responsive to conventional oral disease-modifying antirheumatic drugs, often requiring anti-tumor necrosis factor α agents.
- Further studies are needed to determine the generalizability of these findings to other groups with varying levels of WTC exposure or with other occupational/environmental exposures.

Abstract

OBJECTIVE:

The objective of this study was to describe cases of sarcoid arthritis in firefighters from the Fire Department of the City of New York (FDNY) who worked at the World Trade Center (WTC) site.

METHODS:

All WTC-exposed FDNY firefighters with sarcoidosis and related chronic inflammatory arthritis (n = 11) are followed jointly by the FDNY-WTC Health Program and the Rheumatology Division at the Hospital for Special Surgery. Diagnoses of sarcoidosis were based on clinical, radiographic, and pathological criteria. Patient characteristics, WTC exposure information, smoking status, date of diagnosis, and pulmonary findings were obtained from FDNY-WTC database. Joint manifestations (symptoms and duration, distribution of joints involved), radiographic findings, and treatment responses were obtained from chart review.

RESULTS:

Nine of 60 FDNY firefighters who developed sarcoidosis since 9/11/2001 presented with polyarticular arthritis. Two others diagnosed pre-9/11/2001 developed sarcoid arthritis after WTC exposure. All 11 were never cigarette smokers, and all performed rescue/recovery at the WTC site within 3 days of the attacks. All had biopsy-proven pulmonary sarcoidosis, and all required additional disease-modifying antirheumatic drugs for adequate control (stepwise progression from hydroxychloroquine to methotrexate to anti-tumor necrosis factor α agents) of their joint manifestations.

CONCLUSIONS:

Chronic inflammatory polyarthritis appears to be an important manifestation of sarcoidosis in FDNY firefighters with sarcoidosis and WTC exposure. Their arthritis is chronic and, unlike arthritis in non-WTC-exposed sarcoid patients, inadequately responsive to conventional oral disease-modifying antirheumatic drugs, often requiring anti-tumor necrosis factor α agents. Further studies are needed to determine the generalizability of these findings to other groups with varying levels of WTC exposure or with other occupational/environmental exposures.

References

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