RECEIVED MAR 11 2019
KH

A. Interested Party Information

A1. Do you represent an organization (are you submitting this petition on behalf of an organization)?
☐ Yes (Go to A2) ☒ No (Go to A3)

A2. Organization Information:

Name of organization

A3. Name of Individual Petitioner or Organization Representative:

[redacted] [redacted]
First name Last name

Position, if representative of organization

A4. Mailing Address:

[redacted]
Street

[redacted] [redacted] [redacted]
City State Zip code

A5. Telephone Number: [redacted]

A6. Email Address: [redacted]

B. Proposed WTC-Related Health Condition Information

B1. Health Condition Information:

MGUS - monoclonal gammopathy of undetermined significance
Name of health condition you wish to petition to add to the List of covered conditions

If the name of the condition is not known, please provide a description of the condition or the name of the diagnosis provided by a physician or other healthcare provider.

C. Basis for Proposing that the Condition Be Added to the List of WTC-Related Health Conditions

C1. Describe the reasons the WTC Program Administrator should consider the addition of this health condition. Explain how the health condition you are proposing relates to the exposures that may have occurred from the September 11, 2001, terrorist attacks. Your explanation must include a medical basis for the relationship/association between the 9/11 exposure and the proposed health condition. The medical basis may be demonstrated by reference to a peer-reviewed, published, epidemiologic study about the health condition among 9/11 exposed populations or to clinical case reports of health conditions in WTC responders or survivors. First-hand accounts or anecdotal evidence may not be sufficient to establish medical basis. If you need more space, please attach additional pages to this form.

See attached

D. Signature of Petitioner

Sign your name below to indicate that you are petitioning the WTC Program Administrator to consider adding a health condition to the list of WTC-related health conditions identified in 42 C.F.R. Part 88.

[redacted] [redacted]

Signature Date

Privacy Act Statement

In accordance with the Privacy Act of 1974, as amended (5 U.S.C. § 552a), you are hereby notified of the following:

Title I of the James Zadroga 9/11 Health and Compensation Act of 2010 amended the Public Health Service Act (PHS Act) to establish the World Trade Center (WTC) Health Program. Sections 3311, 3312, and 3321 of Title XXXIII of the PHS Act require that the WTC Program Administrator develop regulations to implement portions of the WTC Health Program established within the Department of Health and Human Services (HHS). The WTC Health Program is administered by the Director of the National Institute for Occupational Safety and Health (NIOSH), within the Centers for Disease Control and Prevention (CDC). The information provided with this form and supporting documentation will be used by the WTC Program Administrator to consider the disposition of a petitioned-for health condition. Disclosure of this information is voluntary.

Records containing information in identifiable form become part of an existing NIOSH system of records under the Privacy Act, 09-20-0147, "Occupational Health Epidemiological Studies and EEOICPA Program Records and WTC Health Program Records, HHS/CDC/NIOSH." These records are treated in a confidential manner, unless otherwise compelled by law.

Information submitted to WTC Health Program which may be considered "protected health information" pursuant to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) (Pub. L. 104–191; 42 U.S.C. § 1320d) and the HIPAA Privacy, Security, Breach Notification, and Enforcement Rules (45 C.F.R. pts. 160, 162, and 164) will be maintained in accordance with all applicable laws.

NIOSH may disclose information in identifiable form only insofar as such disclosure is permitted pursuant to the HIPAA Privacy Rule; this may include disclosure to the WTC Health Program Scientific/Technical Advisory Committee (STAC), which may be asked to consider the petition and issue a recommendation to the WTC Program Administrator. Information in identifiable form will be redacted from submitted petition forms and supporting documentation that become a part of the public record (e.g. in conjunction with STAC consideration or a rulemaking).

PETITION TO ADD MGUS TO WTC-RELATED HEALTH CONDITIONS
FOR COVERAGE UNDER WTC HEALTH PROGRAM

My name is [redacted] and I was a non-union volunteer fireman from [redacted] and then a paid worker for [redacted] at the World Trade Center site for over [redacted]

I worked in and around the following site areas during that time:

[redacted]

During the time that I volunteered and worked at the WTC site I was involved with digging, operating dust suppression water trucks, and debris removal.

The supporting documentation of my work at the WTC site Included in petition are:

- WTC ID card copy
- NYS Workers Compensation Board ID copy, showing Date of Acciden[redacted]
- NYS Crime Victims Board Determination dated 11/9/2007 for Date of Crime 9/11/2001
- Letter dated 1/1/2007 from me (which was sent to NYS Crime Victims Board) listing those who can verify my work time spent in the WTC Rescue Effort.
- 2 pictures of me at the WTC site in my work clothes

- Letter dated [redacted] from the World Trade Center Health Program acknowledging that I am a member of the WTC Health Program
- Letter date[redacted] from the Victim Compensation Fund with my ID/Claim number.
- Letter dated 8/12/2005 from Home Ground – WTC Rescue and Recovery Workers Outreach thanking me for my service at the WTC. I cannot find the certificate.
- Letter dated 11/13/2001 from the President of [redacted] ommending my volunteer efforts at the WTC.

Additional documentation included:

- Report from JAMA Oncology, 4/26/2018 - "Multiple Myeloma and Its Precursor Disease Among Firefighters Exposed to the World Trade Center Disaster"
- Myeloma Research News, 5/7/2018 – "9/11 Firefighters at Greater Risk of Multiple Myeloma Precursor, Study Reports"
- World Trade Center Health Program Scientific/Technical Advisory Committee (STAC) Meeting Minutes, 3/1/2018, page 63 – statement from Dr. Joh Howard, NIOSH, about heightened surveillance for MGUS patients.

[redacted]

In [redacted] after several years of being diagnosed with [redacted] my GP recommended a bone marrow biopsy. The biopsy was performed [redacted] and comprehensive blood tests were done. The results of the biopsy were negative for cancer, but the blood tests showed that I have MGUS. MGUS is a precursor of Multiple Myeloma.

At this time MGUS is not a NIOSH certified condition, however members of the FDNY health coverage program are being monitored for the condition with regular blood tests. [redacted] LHI will not approve my blood tests because MGUS is not a certified condition.

There was a study done by Albert Einstein college of Medicine, Memorial Sloan Kettering, Montefiore Health System, and the NYFD, that determined that 9/11 Firefighters were at greater risk of Multiple Myeloma due to MGUS. The Multiple Myeloma Research Foundation is in agreement that exposure to toxins at the WTC site are at an elevated risk for MGUS. The report and the article are attached.

MGUS is not a certified condition by NIOSH. However, Dr. John Howard of NIOSH has recognized this research and said at a STAC meeting on 3/1/2018 "Our next step is going to be reaching out to these people who are MGUS-positive and offering them a heightened surveillance for multiple myeloma". This excerpt from the minutes of the meeting is attached.

NYFD firefighters who have the disease are part of the heightened surveillance and are receiving the monitoring blood test every 6 months. However, because it is not a certified by

NIOSH, [redacted] I am not accorded the same coverage.

I have discussed with my LHI Case Manager. Since MGUS is a pre-cancerous condition, she suggested that I file this Petition for the Addition of a new WTC -Related Health Condition for Coverage under the WTC Health Program.

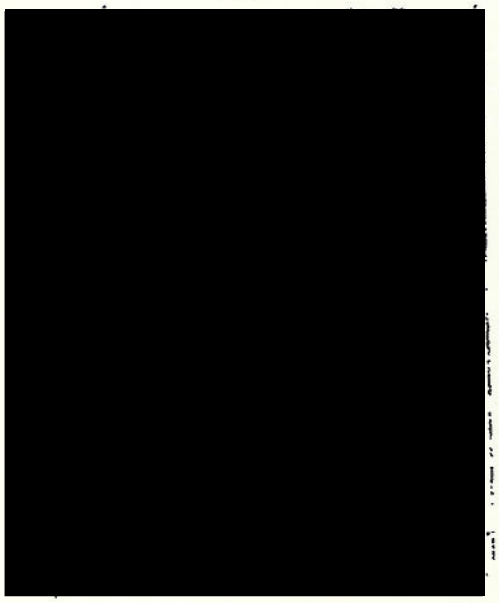
I have also requested help from the 911 Health Watch organization. Mr. Chevat answered that he is "Not really sure what "coverage" would mean as there is NO treatment. Increase monitoring for cancer is I believe what Dr. Howard was talking about and is the protocol now." And then "It is my understanding that those that have this condition do receive increased monitoring including additional blood tests every year to monitor for cancer that the program pays for".

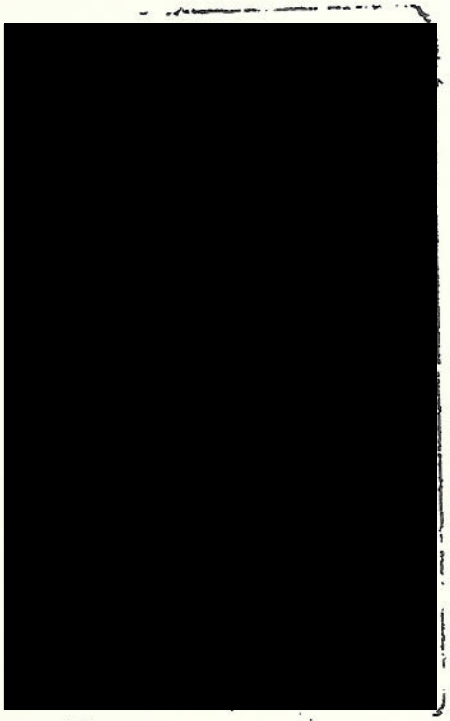
These statements from 911 Health Watch indicate that the heightened surveillance is currently being done, which I interpret to be that MGUS monitoring is being covered by WTCHP. However, those receiving the additional blood tests are in the New York City area and are treated through the NYFD health coverage plan. I was not an employee of the NYFD [redacted] therefore, I am ineligible for the same care that they receive.

This petition is for two reasons:

1. All WTC first responders are entitled to the same level of medical coverage - be it treatment or surveillance.
2. MGUS must be added to the list of certified conditions under the World Trade Center Health Program.

Thank you for your consideration of this proposal and I look forward to a positive outcome. I came forward, as did many others, on 9-11-01 and afterwards because it was the right thing to do, and sincerely hope that you approve this petition.





PQ

Verse (Draft 2-3-03)

1. Usted puede ser atendido de emergencia en el hospital o por un proveedor de salud. Tratamiento posterior debe ser con un proveedor de servicios autorizado, excepto cuando su patrono ha sido autorizado a participar en un programa de gerencia de salud certificado o está en una organización de proveedores preferidos.

2. Solicite a su médico que provea informes médicos a la compañia de seguros y a la Junta de Compensación Obrera.

3. No pague facturas medicas. Si su reclamacion no es cuestionada, la compañia de seguros de su patrono es responsable del pago. Si su reclamación es cuestionada, el proveedor de servicios de salud deberá esperar hasta que la Junta de Compensación Obrera haga una determinacion en el caso. Si usted no cumple con los requisitos para proseguir con su caso o si la Junta desestima su reclamación, le toca a usted la responsabilidad de pagar su factura médica.

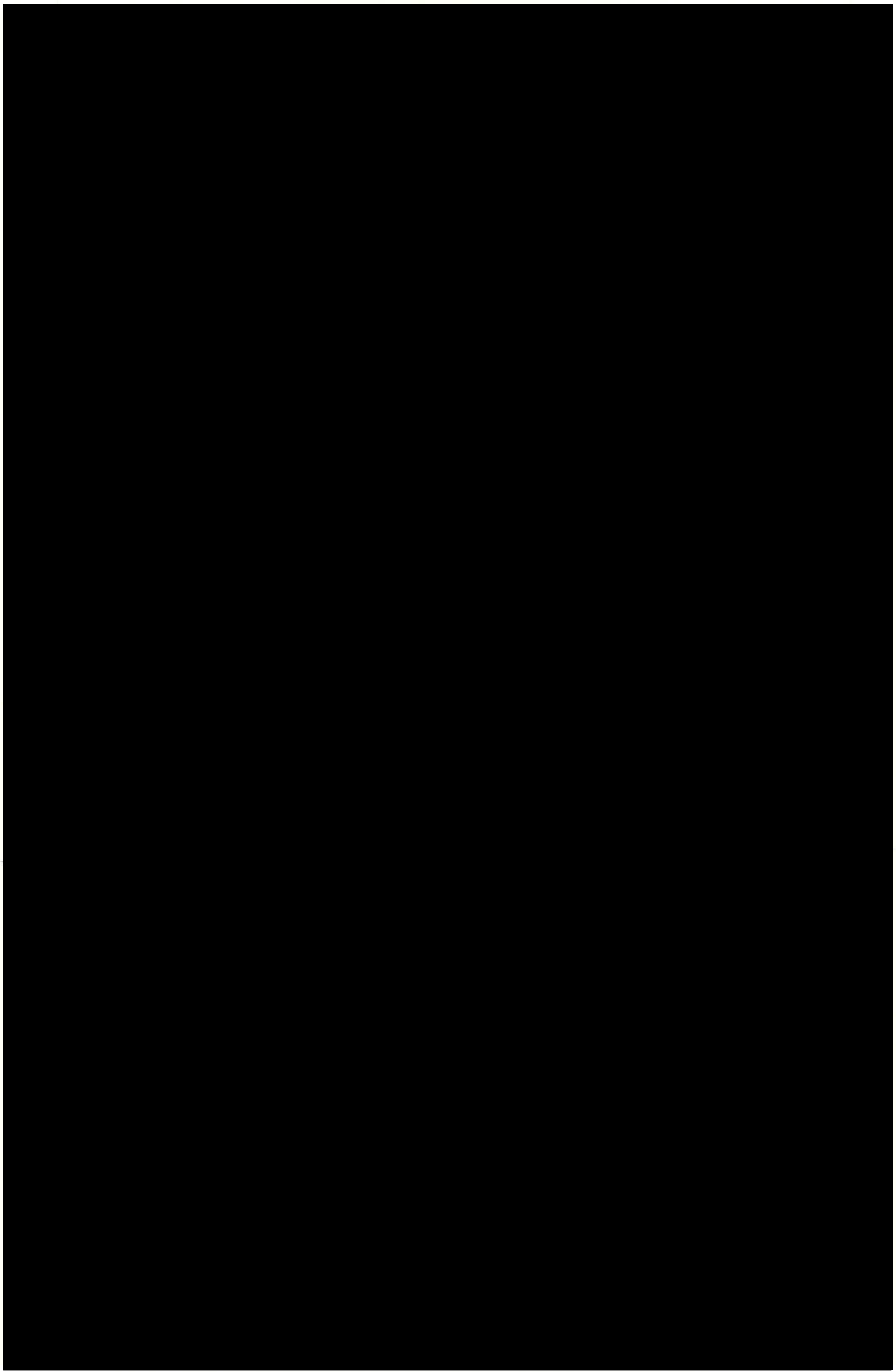
1. You may get emergency treatment from any hospital or health pro... Continuing treatment must be provided by an authorized health provider, ex... if your employer has been approved to take part in a certified managed c... program or is involved in a certifed preferred provider organization.

2. Tell your doctor to file medical reports with the insurance carrier and Workers' Compensation Board.

3. Do not pay any medical bill yourself. If your claim is not disputed, insurance carrier for your employer is responsible to pay the medical bil... your claim is disputed, the health provider must wait for payment pe... determination by the Board. If you fail to pursue your case or it is disallow... the Board, you are responsible for payment of the medical bills.

[redacted]

[redacted]



[redacted]

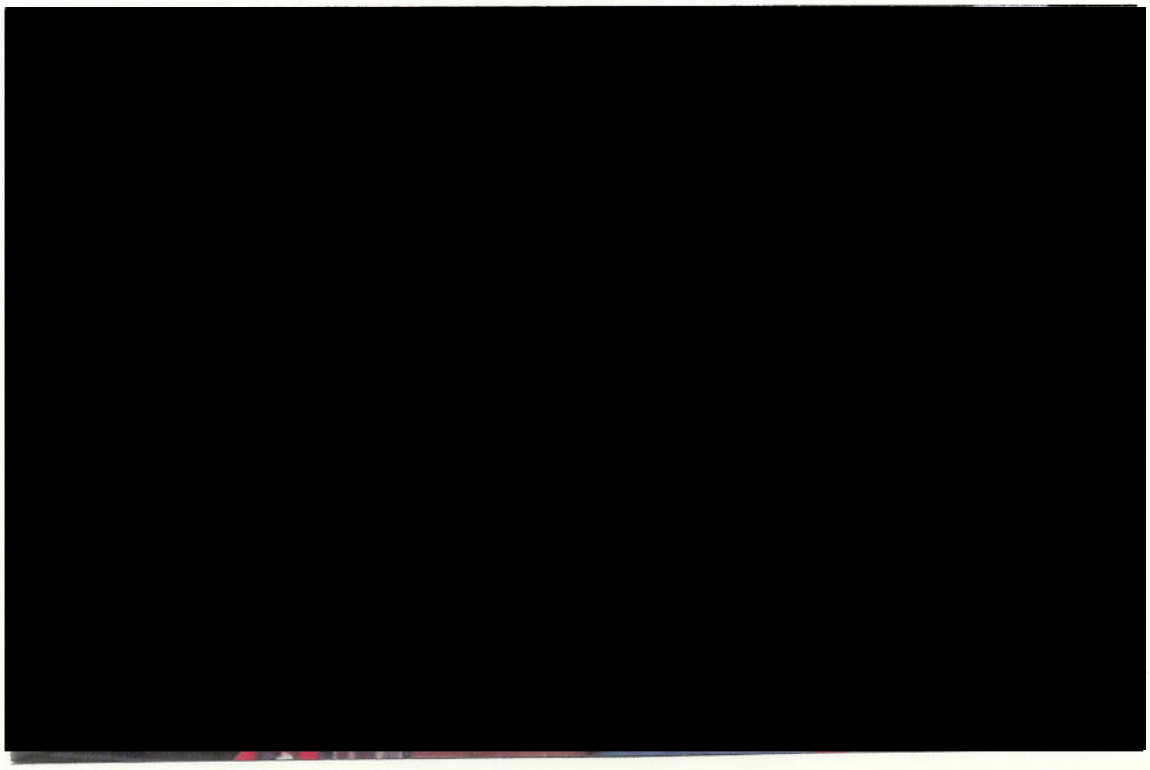
To Whom It May Concern;

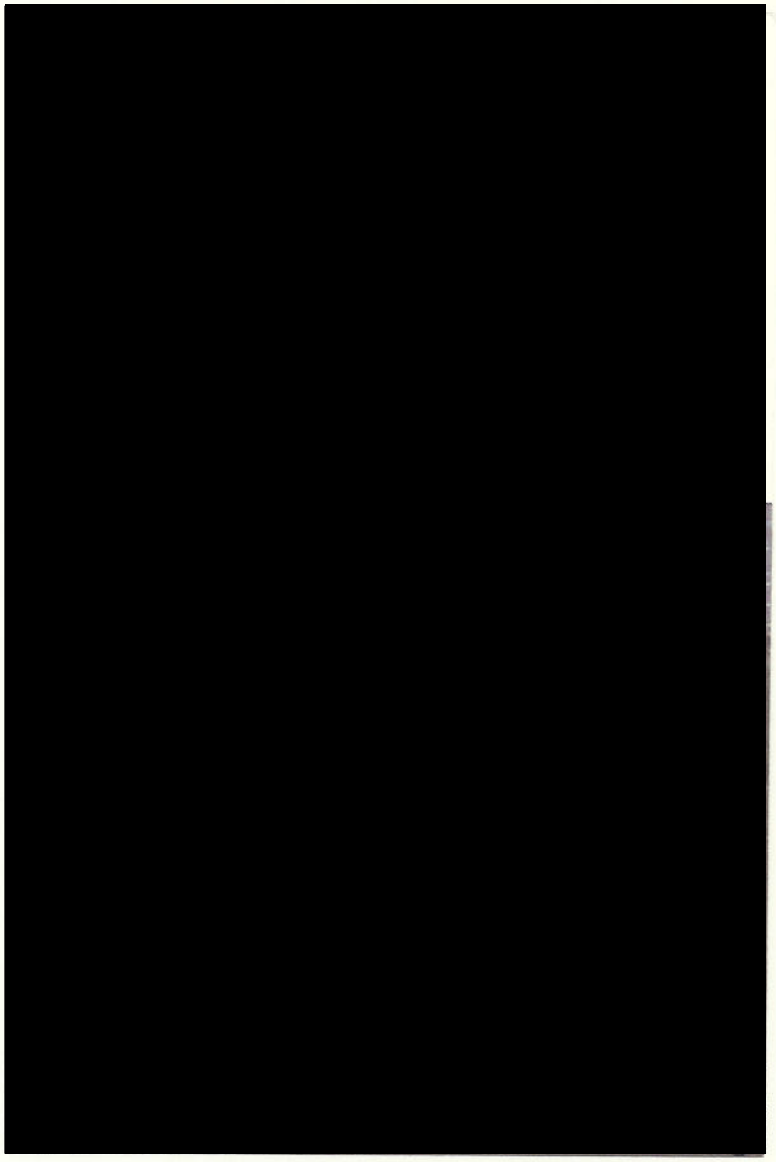
Enclosed is a list of People who can verify I was at the WTC Rescue Effort as a Volunteer

[redacted]

If Any other Information is needed Please Contact me at my Home Address

[redacted]





World Trade Center Health Program
State University of New York, Stony Brook
1345 Motor Parkway, 1st Floor, Islandia NY 11749/Tel. (631) 855-1200/ Fax (631)630-6297
1300 Franklin Ave, Suite 4UL-A, Garden City NY 11530

[redacted]

[redacted]

Dear [redacted]

You are receiving this letter because you are a member of the World Trade Center (WTC) Health Program administered by the National Institute for Occupational Safety and Health (NIOSH) and you are affiliated with the Long Island Clinical Center of Excellence (LI CCE). The Administrator of the WTC Health Program has added several types of cancers to the List of WTC-Related Health Conditions eligible for treatment under the WTC Health Program established by the James Zadroga 9/11 Health and Compensation Act of 2010. A set of frequently asked questions is included with this letter. In the frequently asked questions you will find information about the types of cancer that have been added and what you need to do if you have cancer now or if you want to be screened for certain cancers in the future.

This WTC Health Program change allowing coverage for certain types of cancer becomes effective on October 12, 2012. If you have one of the WTC covered cancers and want to pursue certification, please contact our office and staff will assist you in securing the necessary documentation. The LI-CCE will, with your approval, immediately proceed with making a determination regarding your cancer and submit the required paperwork to the Administrator of the WTC Health Program so that he can decide whether to certify your cancer under this program. Only upon certification by the WTC Program Administrator may cancer treatment be covered under this program.

Screening for breast and colon cancer may be made available as part of the annual monitoring exam benefit through the WTC Health Program using the U.S. Preventive Services Task Force guidelines. Although screening does not require a member to have a certified condition, other eligibility requirements, such as age, may have to be met. Breast and colon screenings will not begin until the WTC Program Administrator further defines these screening eligibility requirements.

We have tried to make the enclosed information as clear as possible. As with any expansion of services, specifics of the program may change as it is rolled out. We will work with you to make this transition as smooth as possible.

If you have questions about anything in this letter, we strongly urge you to consult the LI-CCE WTC Health Program by calling 631-855-1200 and indicate you are inquiring about newly expanded cancer services. You can also contact the NIOSH WTC Health Program member service line at 1-888-982-4748 Monday through Friday, 9 AM to 5 PM (Eastern Time Zone) or visit the WTC Health Program website at: http://www.cdc.gov/wtc.

World Trade Center Health Program

Benjamin J. Luft, MD

September 11th
Victim Compensation Fund

[redacted]

This letter confirms that the September 11th Victim Compensation Fund (VCF) has received the Eligibility Form you submitted on behalf of the individual listed below.

Your claim number is: [redacted]

Please retain this claim number as you will need to provide it on any documents or correspondence that you submit to the VCF by mail. You will also need to provide this claim number if you contact the Helpline for information about your claim or claim status.

This letter is automatically generated when an Eligibility Form is submitted. The VCF has not yet reviewed your claim. One important reminder: If you have not already done so, please mail your original, signed Exhibit A – "Authorization for Release of Medical Records". Exhibit A is the document that we need in order to request information about your claim from other organizations, such as the WTC Health Program. Because these organizations require us to provide original handwritten signatures, we cannot fully process your claim until we receive the original, signed Exhibit A by mail. All other Attestations, Certifications and Exhibits can be uploaded to your online claim or mailed with your Exhibit A to:

September 11th Victim Compensation Fund
P.O. Box 34500
Washington, D.C. 20043

If you have any questions regarding this letter or your claim, please call our toll-free Helpline at 1-855-885-1555. For the hearing impaired, please call 1-855-885-1558 (TDD). If you are calling from outside the United States, please call 1-202-353-0356.

Every effort will be made to respond to your application and/or inquiries as soon as possible.

Sincerely,

September 11th Victim Compensation Fund

[redacted]

[redacted]

I would like to personally thank you, on behalf of South Nassau Communities Hospital's Home Ground program and your fellow Long Islanders, for your efforts during a time of great need following the World Trade Center terrorist attacks.

Please accept the enclosed Certificate of Appreciation to document the honor you received. We will also be presenting you with a gift of a commemorative pin as a small token of the deep respect and gratitude we believe you deserve. Our staff will bring these pins in person to your department. This special recognition permits the Long Island community to share their appreciation for your efforts.

Home Ground is committed to shifting the focus of 9/11 Responders from Ground Zero to Home Ground. We offer free and confidential counseling to 9/11 Responders and their families who need assistance in making that transition. Please call us if you know of anyone that we can support.

Home Ground also believes that Long Islanders should continue to honor the many personal sacrifices that were made during the rescue and recovery efforts. As part of this initiative, we are sponsoring several important projects.

SOUTH NASSAU
COMMUNITIES HOSPITAL
Touching lives, one patient at a time.
A Partner in the Winthrop South Nassau University Health System, Inc
One Healthy Way, Oceanside, NY 11572
1-877-SOUTH-NASSAU • www.southnassau.org
Member
NewYork-Presbyterian Healthcare System

[redacted]

November 13, 2001

[redacted]

On behalf of Teamsters [redacted], we commend you for your volunteer efforts following the World Trade Center tragedy. The numerous hours you donated to render assistance to the fire department, rescue workers and other agencies under the Mayor's Office of Emergency Management and/or to benefit the victims families was a selfless extension of teamster brotherhood to a New York community in dire need.

[redacted] and its members were among the first to mobilize and render aid to "Ground Zero" and other support areas in the metro area. The giving has continued in the form of donated labor to the many charity benefits that have sprung up to assist the loved ones of those who fell. Your ability to react to this crisis and perform critical tasks under the most stressful and horrific of conditions is a credit to you, your families and our union.

In recognition of your service to our community, you will be credited with one pension/welfare/scholarship unit for each day you have volunteered in the coordinated efforts of [redacted]. You have made us proud to be members of [redacted] and we thank you.

Sincerely yours,

Thomas R. O'Donnell

Thomas R. O'Donnell
President

/mm

1. Creation of a "9/11 Responder Registry" of all Long Islanders that served in 9/11 rescue and recovery operations, which is posted on our website www.homeground.org . This roster will serve as an historical record of the important contributions of Long Islanders. Please let us know if we can include your name on this list by filling out the attached consent form and returning it to us in the enclosed stamped self addressed envelope.

2. Videotaping of the stories of 9/11 Responders to be part of an ongoing 9/11 curriculum for our children. We hope to help create a legacy of this tragic event in our history that includes the important perspectives of Long Island Responders.

3. Outreach to other 9/11 Responders who have not been recognized. Home Ground will be available to personally present this recognition wherever the Responder feels most comfortable.

Home Ground and I look forward to speaking with you in the future.

Best Wishes,

Thomas Demaria, Ph.D.
Principal Investigator, "Home Ground"
Assistant Vice-President – Behavioral Health Services

JAMA Oncology | Original Investigation

Multiple Myeloma and Its Precursor Disease Among Firefighters Exposed to the World Trade Center Disaster

Ola Landgren, MD, PhD; Rachel Zeig-Owens, DrPH; Orsolya Giricz, PhD; David Goldfarb, MPH; Kaznouri Murata, PhD; Katie Thoren, PhD; Lakshmi Ramanathan, PhD; Malin Hultcrantz, MD, PhD; Ahmet Dogan, MD, PhD; George Nwankwo, BS; Ulrich Steidl, MD, PhD; Kith Pradhan, PhD; Charles B. Hall, PhD; Hillel W. Cohen, DrPH; Nadia Jaber, PA-C; Theresa Schwartz, MS; Laura Crowley, MD; Michael Crane, MD; Shani Irby, NP; Mayris P. Webber, DrPH; Amit Verma, MD; David J. Prezant, MD

Editorial page 775

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Supplemental content

IMPORTANCE The World Trade Center (WTC) attacks on September 11, 2001, created an unprecedented environmental exposure to known and suspected carcinogens suggested to increase the risk of multiple myeloma. Multiple myeloma is consistently preceded by the precursor states of monoclonal gammopathy of undetermined significance (MGUS) and light-chain MGUS, detectable in peripheral blood.

OBJECTIVE To characterize WTC-exposed firefighters with a diagnosis of multiple myeloma and to conduct a screening study for MGUS and light-chain MGUS.

DESIGN, SETTING, AND PARTICIPANTS Case series of multiple myeloma in firefighters diagnosed between September 11, 2001, and July 1, 2017, together with a seroprevalence study of MGUS in serum samples collected from Fire Department of the City of New York (FDNY) firefighters between December 2013 and October 2015. Participants included all WTC-exposed FDNY white, male firefighters with a confirmed physician diagnosis of multiple myeloma (n = 16) and WTC-exposed FDNY white male firefighters older than 50 years with available serum samples (n = 781).

EXPOSURES WTC exposure defined as rescue and/or recovery work at the WTC site between September 11, 2001, and July 25, 2002.

MAIN OUTCOMES AND MEASURES Multiple myeloma case information, and age-adjusted and age-specific prevalence rates for overall MGUS (ie, MGUS and light-chain MGUS), MGUS, and light-chain MGUS.

RESULTS Sixteen WTC-exposed white male firefighters received a diagnosis of multiple myeloma after September 11, 2001; median age at diagnosis was 57 years (interquartile range, 50-68 years). Serum/urine monoclonal protein isotype/free light-chain data were available for 14 cases; 7 (50%) had light-chain multiple myeloma. In a subset of 7 patients, myeloma cells were assessed for CD20 expression; 5 (71%) were CD20 positive. In the screening study, we assayed peripheral blood from 781 WTC-exposed firefighters. The age-standardized prevalence rate of MGUS and light-chain MGUS combined was 7.63 per 100 persons (95% CI, 5.45-9.81), 1.8-fold higher than rates from the Olmsted County, Minnesota, white male reference population (relative rate, 1.76; 95% CI, 1.34-2.29). The age-standardized prevalence rate of light-chain MGUS was more than 3-fold higher than in the same reference population (relative rate, 3.13; 95% CI, 1.99-4.93).

CONCLUSIONS AND RELEVANCE Environmental exposure to the WTC disaster site is associated with myeloma precursor disease (MGUS and light-chain MGUS) and may be a risk factor for the development of multiple myeloma at an earlier age, particularly the light-chain subtype.

JAMA Oncol. 2018;4(6):821-827. doi:10.1001/jamaoncol.2018.0509
Published online April 26, 2018.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Ola Landgren, MD, PhD, Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065 (landgrec@mskcc.org).

Multiple myeloma is a clonal neoplasm of differentiated B cells (plasma cells). It is one of the most common hematologic malignant neoplasms among adults, affecting approximately 100 000 persons currently living with the disease in the United States, and has an age-adjusted incidence rate of 6.53 per 100 000 per year.[1-3] Multiple myeloma is most frequently diagnosed among people aged 65 to 74 years; only approximately 5% of cases are diagnosed before 50 years.[2] In the general population, approximately 80% of patients with multiple myeloma have expression of IgH (referred to as "monoclonal-(M)-protein") and 20% have abnormal light-chain proteins detectable in peripheral blood.[4] Evidence from a large, prospective, population-based cancer screening trial shows that IgH-secreting and light-chain-secreting multiple myeloma are consistently preceded by their respective precursor states, monoclonal gammopathy of undetermined significance (MGUS) and light-chain MGUS, which can be detected in peripheral blood.[5]

Although the cause of multiple myeloma and its precursor conditions (MGUS and light-chain MGUS) remains largely unclear, previous studies have reported an increased risk among individuals exposed to known and suspected carcinogens including polychlorinated biphenyl (PCB), dioxins, polycyclic aromatic hydrocarbons (PAHs), and asbestos.[6-8] The attacks on the World Trade Center (WTC) on September 11, 2001 (9/11), created an unprecedented environmental exposure to aerosolized dust and gases that contained known carcinogens including PCBs and PAHs.[9] These substances were produced by the collapsed and burning buildings and by the diesel smoke emitted from heavy equipment used during the 10-month rescue and recovery effort. Recent cohort studies of first responders, construction workers, and volunteers at the WTC site provided evidence linking exposure to the WTC aerosolized dust and gases with multiple myeloma and other malignant neoplasms. In 2009, a case series (N = 8) suggested an excess of early-onset of multiple myeloma among WTC-exposed first responders in the General Responder Cohort; 4 of the individuals were 45 years or younger at diagnosis.[10] Since 2011, studies have examined the post-9/11 incidence of multiple myeloma, and other cancers, in 3 WTC-exposed cohorts compared with the general population. A study of 55 778 New York state residents enrolled in the WTC Health Registry (including rescue workers, recovery workers, and those who lived or worked near the WTC) reported a nearly 3-fold (standardized incidence ratio [SIR], 2.85; 95% CI, 1.15-5.88) higher risk of multiple myeloma, based on 7 cases.[11] However, a follow-up study focusing on 10-year cancer incidence patterns in the same population observed a nonsignificant 1.4-fold (SIR, 1.35; 95% CI, 0.70-2.36) increased risk of multiple myeloma.[12] Similar studies among 8927 Fire Department of the City of New York (FDNY) WTC-exposed firefighters reported an SIR of 1.49 (95% CI, 0.56-3.97)[13] while another among 20 984 non-FDNY responders from the General Responder Cohort reported an SIR of 1.41 (95% CI, 0.64-2.67).[14]

To improve our understanding of this association, we identified and characterized all WTC-exposed white, male firefighters from FDNY who received a diagnosis of multiple myeloma from September 12, 2001, to July 1, 2017. Second, we conducted a screening study for myeloma precursor disease among the FDNY subset of 781 white male WTC-exposed firefighters older than 50 years. The aim of our screening study was to define the age-specific prevalence of MGUS and light-chain MGUS in WTC-exposed New York City male firefighters and to compare the FDNY prevalence with that in the male Olmsted County, Minnesota, population. We also assessed patterns of myeloma precursor disease in relation to our exposure metric (time of initial arrival at the WTC site) to test for a possible exposure-response association.

Key Points

Question Are environmental exposures from the World Trade Center disaster site associated with multiple myeloma and its precursor disease, monoclonal gammopathy of undetermined significance (MGUS), in New York City firefighters?

Findings In this case series, 16 participants were diagnosed with multiple myeloma after September 11, 2001, with a median age of disease onset of 57 years, and in subsets with relevant data, a high proportion of the cases had light-chain myeloma, and plasma cells were CD20 positive. In the screening study, World Trade Center exposure was found to be statistically significantly associated with light-chain MGUS and overall MGUS.

Meaning World Trade Center disaster exposures are associated with myeloma precursor disease (MGUS) and may be a risk factor for the development of multiple myeloma at an earlier age.

Methods

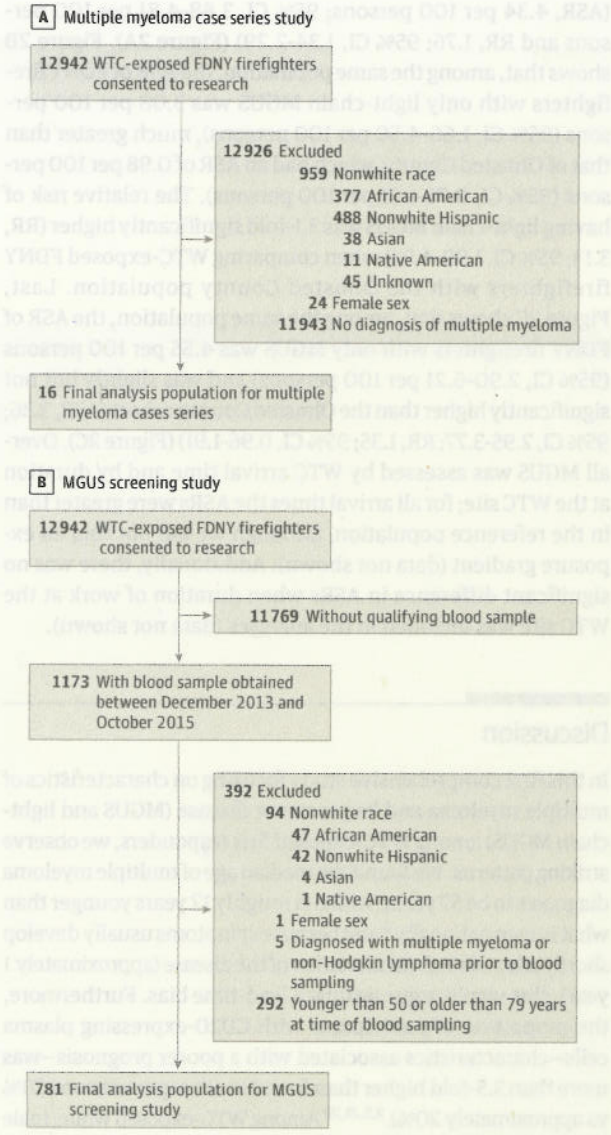
The case series and screening studies were approved by the Institutional Review Boards of Montefiore Medical Center and Albert Einstein College of Medicine. All participants provided written consent to research.

Multiple Myeloma Case Series

Population and Case Information

Through the WTC Health Program, FDNY WTC-exposed firefighters (N = 12 942) receive comprehensive physical and mental health services. All white, male firefighters with a post-9/11 diagnosis of multiple myeloma (n = 16) in the FDNY WTC Health Program as of July 1, 2017, were included in the case series population (**Figure 1A**). The cases were confirmed in 2 ways: (1) via state tumor registry matches with New York, New Jersey, Connecticut, Pennsylvania, Florida, North Carolina, South Carolina, Arizona, and Virginia. A total of 8622 of 8830 (98%) retired FDNY firefighters in this cohort currently reside in these states. All active FDNY firefighters are required to live in New York City or neighboring New York state counties of Westchester, Rockland, Orange, Nassau, or Suffolk; (2) via FDNY WTC Health Program medical assessments/records reviewed by an experienced clinician (N.J.).[13] Using medical records from the time of diagnosis, we extracted information on age at diagnosis, bone marrow aspirate and biopsy reports, and serum and urine protein testing. We performed complete case analysis when outcome data were missing.

Figure 1. Exclusion Criteria



FDNY indicates Fire Department of the City of New York; MGUS, monoclonal gammopathy of undetermined significance; WTC, World Trade Center.

FDNY MGUS Screening Study

Population

The FDNY WTC Health Program provides regular monitoring examinations approximately every 12 to 18 months. From December 2013 through October 2015, serum samples were collected from 1173 WTC-exposed firefighters during routine monitoring examinations (Figure 1b). If a firefighter had more than 1 monitoring examination during the study period, serum was collected from the first examination. To facilitate comparison with our multiple myeloma results and our external comparison group, we restricted the analysis to white men. We excluded specimens from 5 who had received a diagnosis of myeloma or non-Hodgkin lymphoma prior to blood sampling. We also excluded participants younger than 50 or older than 79 years at the time of blood sampling. The final study cohort included 781 white, male, WTC-exposed firefighters (**Table**). All serum samples were analyzed for MGUS or light-chain MGUS in 2016.

Table. Characteristics of World Trade Center (WTC)-Exposed Fire Department of the City of New York (FDNY) White Male Firefighters in the Screening Study and Olmsted County, Minnesota, White Male Cohort

Characteristic	No. (%)	
	WTC-Exposed FDNY Firefighters (N = 781)	Olmsted County (N = 7612)
Age, y		
50-59	482 (61.7)	3450 (45.3)
60-69	225 (28.8)	2554 (33.6)
70-79	74 (9.5)	1608 (21.1)
WTC arrival date, 2001		
Morning of Sep 11	116 (14.9)	0
Afternoon of Sep 11	419 (53.6)	0
Sep 12	125 (16.0)	0
Sep 13-24	112 (14.3)	0
Later than Sep 24	9 (1.2)	0
Time spent at WTC site, mean (SD), mo	3.17 (2.68)	0

Demographic data including age at blood sample collection, race, and sex were obtained from the FDNY employee database. Additionally, data from the first self-administered health questionnaire, which began in October 2001, were used to categorize level of WTC exposure based on initial arrival time (arriving the morning of 9/11 [most highly exposed]; arriving the afternoon of 9/11; arriving September 12, 2001; arriving between September 13 and 24, 2001; and arriving between September 25, 2001, and July 24, 2002 [least exposed], when the WTC site closed) and duration at the WTC site (months in which a participant worked at least 1 day at the WTC site).

Serum Specimen and Laboratory Methods

We obtained a 0.5-mL aliquot for each study participant who consented to the FDNY research protocol. Each aliquot tube was labeled only with the participant's coded identification number. All specimens were shipped on dry ice to the Protein Laboratory at Memorial Sloan Kettering Cancer Center, where protein assays were performed. The samples were tested concurrently and results were assessed by 2 of us (O.L. and K.M.) in a blinded fashion.[5,15-17]

Comparison Population: Olmsted County, Minnesota

We used published data from the population-based Olmsted County, Minnesota, study, the only available screening study including both MGUS and light-chain MGUS assays,[18] as our comparison population. The racial distribution of the population in Olmsted County is predominantly white.[19] We focused on the Olmsted County MGUS and light-chain MGUS rates in men 50 to 79 years old (N = 7612). Among the 7612 men, the prevalence of overall MGUS (ie, MGUS and light-chain MGUS), MGUS, and light-chain MGUS was 4.4% (n = 333), 3.4% (n = 258), and 1.0% (n = 75), respectively.[18]

Statistical Analysis

The crude age-specific prevalence rates were calculated for white men as the total number of cases within each age stratum divided

by the total number of individuals within that age stratum. Prevalence rates for overall MGUS, MGUS, and light-chain MGUS were calculated for the FDNY study population. Additionally, to enable external comparison, prevalence rates were age standardized to the US 2000 male population, ages 50 to 79 years. Age-adjusted 95% confidence intervals were calculated for directly standardized relative rates (RRs) using the modified γ approximation method, which assumes a Poisson distribution. Standard errors for 95% Mantel-Haenszel confidence limits of standardized relative risks were calculated using the Greenland and Robins[20] variance formula. Participants older than 79 years were excluded from this analysis due to small numbers in the firefighting cohort. Exposure to the WTC, using time of arrival at the WTC site as a proxy for intensity, was evaluated separately in a stratified analysis. All analyses were performed using SAS, version 9.4, and R v.3.2.0.

Results

Multiple Myeloma Case Series

We identified 16 white male responders from the FDNY firefighter cohort with a post-9/11 diagnosis of multiple myeloma. The median age at diagnosis was 57 years (range, 38-76 years). The median time between 9/11 and diagnosis was 12.0 years (range, 1.0-15.7 years). The myeloma cell infiltration of the bone marrow ranged between less than 10% and 90% across individuals; immunophenotypic characterization of the bone marrow sample revealed CD20-positive plasma cells in 5 of 7 (71%; 95% CI, 36%-92%) tested cases. Results on serum and/or urine monoclonal proteins isotype and free light chains were available for 14 cases; 7 (50%; 95% CI, 27%-73%) had light-chain multiple myeloma. Individual-level data for the case series, including plasma-cell percentage, serum and/or urine monoclonal protein isotype and free light chains, and plasma-cell CD20 expression are provided in eTable 1 in the Supplement.

MGUS Screening Study Demographic Characteristics

The Table provides selected demographic characteristics of the FDNY firefighter cohort and Olmsted County comparison population. The median age at time of FDNY specimen collection was 57 years (interquartile range, 54-62 years). The majority of firefighters arrived at the WTC site on the day of the attacks (535 [68.5%]) and spent a mean (SD) 3.17 (2.68) months working at the WTC site. The Olmsted County cohort was assumed to have no WTC exposure. The median age of firefighters with MGUS was nonsignificantly younger than that among the reference population: 62 years (FDNY firefighter cohort) vs 70 years (Olmsted County comparison population). Similarly, firefighters with light-chain MGUS were nonsignificantly younger than the reference population (median age, 61 vs 68 years). Specific characteristics of MGUS are found in eTable 2 in the Supplement.

MGUS and Light-Chain MGUS Age-Standardized and Relative Rates

Among white men aged 50 to 79 years, the age-standardized prevalence rate (ASR) of overall MGUS among WTC-exposed FDNY firefighters was 7.63 per 100 persons (95% CI, 5.45-9.81), which was 1.8-fold significantly higher compared with the rate among those from Olmsted County, Minnesota (ASR, 4.34 per 100 persons; 95% CI, 3.88-4.81 per 100 persons and RR, 1.76; 95% CI, 1.34-2.29) (**Figure 2A**). Figure 2B shows that, among the same population, the ASR of FDNY firefighters with only light-chain MGUS was 3.08 per 100 persons (95% CI, 1.66-4.50 per 100 persons), much greater than that of Olmsted County, which had an ASR of 0.98 per 100 persons (95% CI, 0.76-1.21 per 100 persons). The relative risk of having light-chain MGUS was 3.1-fold significantly higher (RR, 3.13; 95% CI, 1.99-4.93) when comparing WTC-exposed FDNY firefighters with the Olmsted County population. Last, Figure 2C shows that, among the same population, the ASR of FDNY firefighters with only MGUS was 4.55 per 100 persons (95% CI, 2.90-6.21 per 100 persons) and was slightly but not significantly higher than the Olmsted County cohort (ASR, 3.36; 95% CI, 2.95-3.77; RR, 1.35; 95% CI, 0.96-1.91) (Figure 2C). Overall MGUS was assessed by WTC arrival time and by duration at the WTC site; for all arrival times the ASRs were greater than in the reference population, although we did not find an exposure gradient (data not shown). Additionally, there was no significant difference in ASRs when duration of work at the WTC site was included in the analyses (data not shown).

Discussion

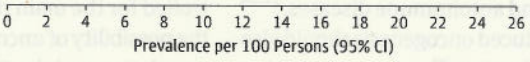
In this first comprehensive study focusing on characteristics of multiple myeloma and its precursor disease (MGUS and light-chain MGUS) among WTC-exposed first responders, we observe striking patterns. We found the median age of multiple myeloma diagnosis to be 57 years, which is roughly 12 years younger than what is seen nationally,[2] and because symptoms usually develop shortly after clinical manifestation of the disease (approximately 1 year), this would argue against a lead-time bias. Furthermore, the proportion of participants with CD20-expressing plasma cells—characteristics associated with a poorer prognosis—was more than 3.5-fold higher than found in other populations (71% vs approximately 20%).[2,5,21,22] Among WTC-exposed white, male firefighters, the proportion of light-chain multiple myeloma was more than double that of the general population (50% vs approximately 20%).[4] Similarly, in our screening study, we found a 2-fold significantly higher risk of myeloma precursor disease, particularly light-chain MGUS, the precursor of light-chain multiple myeloma.[5] As suggested previously based on smaller numbers,[10-14] our study shows that WTC exposure may be a risk factor for the development of multiple myeloma and its precursor disease.

Prior studies in cohorts without WTC exposure have found an increased risk of MGUS and light-chain MGUS among individuals exposed to known and suspected carcinogens including PCB, dioxins, PAHs, and asbestos,[6-8] including exposure to Agent Orange (which contains the human carcinogen 2,3,7,8-tetrachlorodibenzo-p-dioxin).[6] Interestingly, among veterans exposed to Agent Orange who were found to have myeloma precursor disease, there was a particular excess risk of light-chain MGUS (11 of 34 [32%] of the MGUS cases were light-chain MGUS).[6]

Figure 2. Prevalence of Monoclonal Gammopathy of Undetermined Significance (MGUS) and Light-Chain MGUS in World Trade Center–Exposed Fire Department of the City of New York (FDNY) White Male Firefighters and Comparison Population

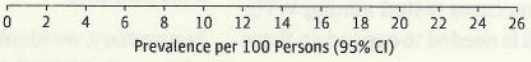
A Overall MGUS prevalence[a]

Age, y	Cases	Total	Prevalence per 100 Persons (95% CI)
50-59			
FDNY	18	482	3.73 (2.01-5.46)
Olmsted County	95	3450	2.75 (2.20-3.31)
60-69			
FDNY	17	225	7.56 (3.96-11.15)
Olmsted County	122	2554	4.78 (3.93-5.62)
70-79			
FDNY	12	74	16.22 (7.04-25.39)
Olmsted County	116	1608	7.21 (5.90-8.53)
Age standardized[b]			
FDNY	47	781	7.63 (5.45-9.81)
Olmsted County	333	7612	4.34 (3.88-4.81)



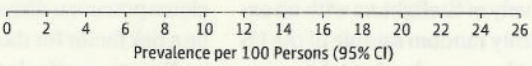
B Light-chain MGUS prevalence

Age, y	Cases	Total	Prevalence per 100 Persons (95% CI)
50-59			
FDNY	9	482	1.87 (0.65-3.09)
Olmsted County	22	3450	0.64 (0.37-0.90)
60-69			
FDNY	3	225	1.33 (0-2.84)
Olmsted County	25	2554	0.98 (0.60-1.36)
70-79			
FDNY	6	74	8.11 (1.62-14.60)
Olmsted County	28	1608	1.74 (1.10-2.39)
Age standardized[b]			
FDNY	18	781	3.08 (1.66-4.50)
Olmsted County	75	7612	0.98 (0.76-1.21)



C MGUS prevalence

Age, y	Cases	Total	Prevalence per 100 Persons (95% CI)
50-59			
FDNY	9	482	1.87 (0.65-3.09)
Olmsted County	73	3450	2.12 (1.63-2.60)
60-69			
FDNY	14	225	6.22 (2.96-9.48)
Olmsted County	97	2554	3.80 (3.04-4.55)
70-79			
FDNY	6	74	8.11 (1.62-14.60)
Olmsted County	88	1608	5.47 (4.33-6.62)
Age standardized[b]			
FDNY	29	781	4.55 (2.90-6.21)
Olmsted County	258	7612	3.36 (2.95-3.77)



[a] Overall MGUS includes both MGUS and light-chain MGUS cases.

[b] Prevalence rates are age standardized to US 2000 male population age 50 to 79 years.

In our multiple myeloma case series, we found 7 of 14 (50%) cases to be of light-chain multiple myeloma subtype, which is more than double the rate in other populations (50% vs approximately 20%).[4] In our screening study, we observed 18 of 47 (38%; 95% CI, 26%-53%) of the precursor cases to have light-chain MGUS, the precursor of light-chain multiple myeloma. Furthermore, we found that the risk of having light-chain MGUS was 3 times higher (RR, 3.13; 95% CI, 1.99-4.93) among our population compared with the Olmsted County population. These findings are of interest due to previously observed associations be-

tween light-chain multiple myeloma and light-chain MGUS and exposure to toxins[6,17] and chronic immune stimulation.[23]

Many WTC first responders were initially exposed to aerosolized dust and toxic fumes from burning jet fuel and building materials. For the next 10 months of the rescue, recovery, and cleanup effort, responders were exposed to burning subterranean fires that released trapped gases and dust, and were not extinguished until the end of December. The final insult included diesel fuel combustion byproducts from heavy equipment used at the site. The WTC dust itself included pulverized cement, glass fibers, asbestos, lead, PAHs, PCBs, and polychlorinated furans and dioxins produced as combustion byproducts from the collapsed and burning buildings.[9] Many of these substances are known carcinogens, providing biologic plausibility for an association between WTC exposure and cancer.[9,24-26] Although some contaminants could directly cause cancer, WTC exposure has been shown to trigger chronic inflammation resulting in upper and lower respiratory diseases and autoimmune diseases,[27-29] and, therefore, inflammation-induced oncogenesis should also be considered as a potential mechanism.[23]

Several surface antigens are used to characterize individual plasma cells as malignant or normal. For example, compared with normal plasma cells, abnormal plasma cells tend to be low in the expression of CD19 and CD27, have weaker expression of CD45, and increased expression of CD28, CD56, and CD117.[30] Expression of CD20 is typically seen during the maturation process of B cells and absent from plasma cells; however, CD20 expression can be detected in 13% to 22% of patients with multiple myeloma diagnosed in the general population.[22] Preliminary data suggest that subsets of CD20-positive multiple myeloma patients have a poorer prognosis.[5,21] In the present study, albeit based on small numbers, immunophenotypic characterization revealed CD20-positive plasma cells in 5 of 7 (71%) multiple myeloma cases tested among WTC-exposed responders. Future work is needed to expand on these observations.

Limitations

We acknowledge that our study has limitations. First, in our myeloma case series analysis, we were not able to rigorously compare FDNY and national age-adjusted incidence rates due to small or zero counts in certain age strata. This is often a challenge in the study of rare cancers.[31] Additionally, when MGUS was assessed by WTC arrival time,[32] for all arrival times the ASRs were greater than in the reference population. However, the study was underpowered to detect an exposure-response gradient association between WTC exposure and MGUS. Nonetheless, we did observe an elevated risk of overall MGUS and light-chain MGUS compared with the Olmsted County population. While a comparison group composed exclusively of firefighters with no exposure to the WTC disaster or a truly random sample of the US population would be most desirable, no such cohort data were available. Specifically, no other study meeting those criteria screened all participants for light-chain MGUS in the same manner that we did. The Olmsted County population matched our testing protocol and was demographically similar and thus provided a valuable comparison for this study. Similarly, due to small numbers in the firefighter cohort and lack of an adequate comparison population, races other than white and women were excluded. Future research investigating MGUS and light-chain MGUS may provide additional comparisons to our full population, as well as other WTC-exposed populations, important populations in need of follow-up.

Furthermore, in our case series analysis it is possible that the onset of precursor disease states may have preceded WTC exposure; however, 75% of myeloma cases were diagnosed more than 5 years after 9/11, with half being at least 12 years following the attacks. This suggests that, for most, the precursor disease likely developed after 9/11.[33] Last, while we controlled for the main risk factors for MGUS, we cannot rule out the possibility of uncontrolled confounding between the FDNY population and the Olmsted County population.

This study had a number of strengths. First, we believe that our case ascertainment was excellent; this included matching to tumor registries where more than 98% of our cohort reside, as well as full access to the FDNY electronic medical record where approximately 87% have had a monitoring or treatment visit within the past 2 years. Second, to our knowledge, this is the largest study to characterize multiple myeloma in WTC-exposed responders. More importantly, this is the first study to establish the age-specific prevalence of MGUS/light-chain MGUS in a well-defined population of WTC-exposed responders.

Conclusions

In summary, we identified and characterized all WTC-exposed white, male FDNY firefighters who received a diagnosis of multiple myeloma from September 12, 2001 to July 1, 2017, and 50% (7 of 14) of these cases were light-chain multiple myeloma. The median age at multiple myeloma diagnosis was 57 years, which is 12 years younger than what is observed in national data.[2] A high proportion of patients with multiple myeloma had CD20-expressing plasma cells, which is a characteristic associated with a poorer prognosis.[5,21] In the screening study including 781 white male WTC-exposed FDNY firefighters, we found the risk of overall MGUS to be 2-fold higher compared with the rate in the Olmsted County reference population; in particular, the risk of light-chain MGUS was higher, which may have important prognostic implications. Taken together, our results show that environmental exposure due to the WTC attacks is associated with myeloma precursor disease (MGUS and light-chain MGUS) and may be a risk factor for the development of multiple myeloma at an earlier age, particularly the light-chain subtype.

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Study supervision: Landgren, Zeig-Owens, Giricz, Steidl, Hall, Webber, Prezant.

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9/11 Firefighters at Greater Risk of Multiple Myeloma Precursor, Study Reports

myelomaresearchnews.com/2018/05/07/9-11-firefighters-greater-mgus-risk-study/

Jose Marques Lopes, PhD

May 7, 2018

New York City firefighters exposed to the 9/11 World Trade Center (WTC) disaster are at greater risk for developing a condition called monoclonal gammopathy of undetermined significance (MGUS), which may lead to multiple myeloma, a study suggests.

The study, "Multiple Myeloma and Its Precursor Disease Among Firefighters Exposed to the World Trade Center Disaster," appeared in the journal *JAMA Oncology*.

Fire Department of the City of New York (FDNY) firefighters and other 9/11 first responders were exposed to unprecedented levels of compounds such as polycyclic aromatic hydrocarbons, dioxins, polychlorinated biphenyls, asbestos, and other potential carcinogens. They were also exposed to significant levels of diesel smoke from the heavy machinery used in the 10-month rescue and recovery effort.

MGUS is characterized by the presence of an abnormal protein called monoclonal, or M, protein, which can be detected with blood tests. Prior research indicated that exposure to toxic chemicals caused the development of both MGUS and multiple myeloma.

"We were the first to show that first responders were more likely to get many different types of cancer," David J. Prezant, MD, one of the study's senior authors, said in a press release. Prezant is a professor of medicine at Albert Einstein College of Medicine and FDNY's chief medical officer.

"We carried out this new study to do more than just treat cancer. We wanted to find early, predictive signs of cancer that would allow us to screen people and monitor those found to be at risk. By detecting MGUS, which predicts the development of multiple myeloma, we are able to do that," he said.

Researchers collected blood samples from 781 white, male firefighters ages 50 to 79, who were exposed to the WTC rescue and/or recovery work between Sept. 11, 2001, and July 25, 2002. Compared with a control group that included non-exposed men from Olmstead County, Minnesota, the prevalence of MGUS in WTC firefighters was almost double (7.63 cases per 100 firefighters versus 4.34 cases per 100 controls).

"We saw a significantly higher incidence of MGUS in these first responders, and they're developing it at a young age," said Amit Verma, another of the study's senior co-authors. Verma further observed that this early development of MGUS suggests an increased risk for early-onset multiple myeloma.

"Taken together, our results show that environmental exposure due to the WTC attacks is associated with myeloma precursor disease," the investigators wrote in the study.

The scientists also analyzed 16 cases of multiple myeloma diagnosed between Sept. 12, 2001, and July 1, 2017, among white, male WTC-exposed firefighters, with an average age of diagnosis of 57. This is 12 years younger than the average age in the U.S. for multiple myeloma diagnosis.

Of note, 7 out of 14 analyzed firefighters had light-chain multiple myeloma. Prior research indicated that this disease subtype is more common after chemical or inflammatory exposures.

As a result of their findings, the scientists recommend screening WTC first responders for both conditions. "Screening for multiple myeloma risk by testing for MGUS is something we can offer these first responders, which is why this study is important," Prezant said.

In an editorial comment, "Some Thoughts on Exposure to the World Trade Center Wreckage and Cancer," Otis W. Bradley, MD, observed that as the firefighting profession has a greater overall risk of MGUS and multiple myeloma, 9/11 responders should have been compared with firefighters from another big city, a limitation the study's own authors acknowledge.

He also wrote that the greater prevalence in 9/11 firefighters may have been due to more intensive screening of MGUS in WTC-exposed personnel. Bradley also cautioned that correlation does not mean causation.

A different study, "Estimation of Future Cancer Burden in World Trade Center-Exposed Fire Department of the City of New York Rescue/recovery Workers," also published in *JAMA Oncology*, predicted how many cancer cases will be diagnosed among FDNY personnel exposed to the WTC disaster, including rescue and recovery workers, between 2012 and 2031.

Results indicate a projected total of 2,714 new cases among white males, particularly cancers of the prostate, thyroid, and melanoma. This estimate shows a greater cancer burden than the 2,596 predicted cancer cases in a similar, non-exposed population. Scientists estimate that the costs for the first year of cancer treatment for these workers will total more than $235 million.

The researchers said all these people need continued careful surveillance and said the program needs to keep funding up to levels that can take care of them.

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So MGUS is a precursor for multiple myeloma. It's also a precursor for some autoimmune diseases, but it's mostly associated with being a precursor for multiple myeloma. And as I said to you, some of the hematologic malignancies seem to be increased. One of those that we're getting a signal for is multiple myeloma. So we collaborated with the National Cancer Institute and then with Sloan Kettering and with Albert Einstein with philanthropy money from the Jimmy V Foundation to get more blood on all of our firefighters and on a subsection of them, send them over to originally was going to go to the National Cancer Institute but that lead physician moved to Sloan Kettering, so it went to Sloan Kettering and he did the analyses.
Next slide. And this has just been accepted.
Next slide. I think I have animation. Next slide and hold it there. This has been accepted in JAMA oncology. And basically what this shows is that MGUS is a predictor for multiple myeloma, as we would know, but that this is occurring at an earlier age than in the general population. And not shown on this slide, the type of multiple myeloma that is being found in our group is light chain multiple myeloma. And light chain multiple myeloma is less common than heavy chain. It also has a far worse prognosis, and importantly, there's a scientific literature that shows that light chain is associated with various different exposures that have occurred, toxicologic exposures that have occurred in the past. So there's a lot of bio-plausibility for this, and this study moves to showing that.
Our next step is going to be reaching out to these people who are MGUS-positive and offering them a heightened surveillance for multiple myeloma. This is all about what I've been saying, which is now from roughly 2017 forward, our focus at FDNY is not just to be able to characterize, but to be able to identify the vulnerable groups, all right, and offer them something necessary to hopefully deal with their vulnerability.