

**Case Report**

# Mesothelioma Cases in the World Trade Center Survivors

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## Abstract

**Objectives:** The destruction of the World Trade Center (WTC) towers in New York City on September 11, 2001 (9/11), released approximately 1 million tons of pulverized particulate matter throughout southern Manhattan and areas in Brooklyn, exposing community members and responders to high levels of potentially toxic environmental particles. Asbestos exposure was a health concern because of its use in certain sections of the WTC towers. Malignant mesothelioma, originating from the lining cells (mesothelium) of the peritoneal and pleural cavities, is one complication associated with asbestos exposure. **Methods:** The WTC Environmental Health Center (WTC EHC) is a treatment and surveillance program for community members (Survivors) exposed to WTC dust and fumes. **Results:** In this report, we describe four cases of mesothelioma in the WTC EHC as of July 1st, 2023. Two of our patients have been diagnosed with peritoneal mesothelioma and two patients have been diagnosed with pleural mesothelioma. **Conclusion:** Given the known delay in the development of mesotheliomas after asbestos exposure, we provide information on these early mesothelioma cases to enhance the understanding of the adverse health effects of WTC exposures on the local community.

**Keywords:** World Trade Center (WTC); WTC Environmental Health Center; September 11th; Mesothelioma

## Introduction

The attack on the World Trade Center (WTC) towers in New York City on September 11, 2001, with the destruction of the towers and neighboring buildings, resulted in the release of more than a million tons of dust and debris into the surrounding air, exposing responders and community members to respirable toxins with the potential for a wide range of adverse health outcomes [1]. The collapse of the towers resulted in dust clouds that dispersed pulverized particulates, including lead, glass fibers, and asbestos, among other chemicals, throughout lower Manhattan [1-4]. Asbestos, the commercial name for a group of hydrated magnesium silicate fibrous minerals, has been commonly used in industry for its resistance to heat and combustion [5]. The exact quantity of asbestos used in the WTC towers can only be estimated, as the original plans were difficult to access. Although use of asbestos was common in buildings, by 1970, during the construction of the WTC towers, spraying of asbestos for insulation became prohibited by New York City. Asbestos, predominantly in the form of chrysotile, was initially incorporated into the construction of the WTC North tower [6,7]. Subsequently, its use was discontinued beyond a certain point due to acknowledged health hazards, with non-asbestiform fireproofing materials implemented for the remaining segments. Although some of this asbestos had been removed over the preceding 30 years, hundreds of tons remained on 11 September 2001 and were blasted free [1-3].

The results of asbestos testing in the surrounding areas have been debated. Of the 10,000 ambient air samples collected by the U.S. Environmental Protection Agency (EPA) from lower Manhattan following 9/11, 22 were found to contain asbestos levels above the Asbestos Hazard Emergency Response Act standard of 70 fibers/mm<sup>2</sup>, with the most elevated levels of asbestos found in samples from the first days following 9/11. Ambient air samples showed that asbestos exposures were initially elevated but fell to within U.S. EPA standards after the first few days [8]. Asbestos was found in settled dust at Ground Zero in concentrations ranging from 0.8 to 3.0% [1]. Asbestos was found in dust in nearby apartments, sometimes at higher levels than in the outside environment [1,8]. Testing of 57 apartments by the Agency for Toxic Substances and Disease Registry was summarized in a report by the EPA in which airborne fibers were reported as not detected above background levels [8]. However, 16% of the apartments in lower Manhattan compared to those more distant, had asbestos in the bulk dust samples [3]. The WTC dust was also known to become airborne with minimal mechanical disturbance [3] and a study of a nearby commercial building showed significant quantities of respirable asbestos, which increased as a function of surface contamination.

Thus, although few studies reported elevated levels of asbestos in measured dust, the known use of asbestos in the towers, the variability of the measurements, the potential for resuspension of dust with potential to re-contaminate areas, and the known health hazards of asbestos made asbestos exposure a health concern following 9/11.

The WTC EHC began as an academic-community partnership funded by philanthropic funds. It was eventually incorporated as a Center of Excellence for the treatment and surveillance of community members (Survivors) under the WTC Health Program (WTC Health Program) formed by H.R. 847 James Zadroga Health and Compensation Act [9]. The WTC EHC enrolls patients with a history of acute WTC dust exposure on 9/11, or chronic exposures within the subsequent year and a defined WTC-related condition, including aerodigestive disorders, and a wide variety of cancers [10,11]. The latency period for inclusion as a WTC-certifiable cancer is defined by the time between exposure to WTC dust and the date of the individual's initial diagnosis of cancer. The minimum latency period for mesothelioma has been determined by the WTC Health Program to be 11 years, based on direct observation after exposure to mixed forms of asbestos (NIOSH) [12]. We have previously described the distribution of cancers in patients in the WTC EHC [13,14]. We now describe four cases of mesothelioma in the WTC-exposed community population as of July 1st, 2023.

## Methods and Data Collection

Individuals qualify for inclusion in the WTC Health Program after an initial health evaluation (IHE) based on exposure criteria outlined by the Centers for Disease Control (CDC)-National Institute of Occupational Safety and Health (NIOSH) [12]. These criteria encompass geographic location, including being present in the dust or dust cloud in the New York City disaster area on September 11, 2001, having worked, resided, or attended school/daycare in that area, engaging in cleanup or maintenance work, and having documented residence or employment within defined timeframes [10]. Additionally, enrollees must have a certifiable WTC-related health condition, which could involve aerodigestive disorders, cancer, or mental health symptoms consistent with PTSD, depression or anxiety [10]. Ongoing monitoring of patients in the WTC EHC is offered approximately every 12–18 months. During the IHE and monitoring visits, patients undergo standardized evaluations including medical and mental health assessments, and documentation of cancer diagnoses. All cancer diagnoses are confirmed through clinical and pathologic records [13,14]. Information is maintained in the WTC EHC Database and the WTC EHC Pan Cancer Database. Mesothelioma characteristics and obtainable biomarker profiles are derived from the WTC EHC Pan-Cancer database and additional information was captured

from review of the medical records.

For this analysis, we include four patients enrolled in the WTC EHC with a diagnosis of mesothelioma between September 2012 (accepted latency period for mesothelioma in WTC EHC) and July 1st, 2023. The study was approved by the New York University School of Medicine Institutional Review Board (IRB number: i06-1 and i06-1\_MOD49) and participants who have signed consent for analysis of their data or who are deceased were included in the study.

## Case Presentation

### Case 1

An 80-year-old female presented with progressive abdominal wall hardening and left lower abdominal pain that began in February 2020. She reported unexplained weight loss and a PET/CT revealed diffuse heterogeneous increased uptake

along the left rectus abdominis muscle, which was asymmetrically enlarged. Subsequently, an image-guided biopsy was performed, which was suspicious for mesothelioma. The patient reported increasing firmness in her lower left abdomen in August 2020. An open biopsy was performed in January 2021 to obtain more tissue, which confirmed unresectable epithelioid mesothelioma of the peritoneum and involvement of the left rectus sheath, diaphragm, serosa, and the small bowel. The latency period was 19 years from the initial WTC dust exposure. Her biomarker profile included positive results for WT1, calretinin, D2-40, BER-EP4 and, mesothelin (95%). The tumor was negative for BAP-1, CEA and PDL-1 (Table 1, 3). The patient planned to begin chemotherapy at the time. The patient's relevant past surgeries included three cesarean sections between 1973 and 1980, a cholecystectomy in 2003, and an appendectomy as a child. Additionally, the patient had no family cancer history and had squamous cell carcinoma of the skin cancer with excision in 2015.

	Case 1	Case 2	Case 3	Case 4
Sex	Female	Male	Male	Male
Age on 9/11 (years)	60	23	53	38
Race	Unknown	White	White	White
Ethnicity	Hispanic	Non-Hispanic	Non-Hispanic	Non-Hispanic
Country of origin	Peru	USA	USA	USA
BMI	24	21.3	29.8	Unknown
Income	more than \$30,000/year but less than \$50,000/year	more than \$50,000/year	more than \$50,000/year but less than \$100,000/year	more than \$100,000/year
Education	More than high school	4-year college degree	High school (12th grade)	More than 4-year college degree
Outcome (deceased/alive)	Alive	Alive	Deceased	Deceased
Date of death	Not applicable	Not applicable	2019	2022

WTC EHC: World Trade Center Environmental Health Center

**Table 1:** Characteristics of patients with mesothelioma in the WTC EHC.

The patient worked as an office cleaner in lower Manhattan and on 9/11/2001 she reported acute exposure to the WTC dust. She returned to work at the same location one week after 9/11 and would work 40 hours a week. Typically, she would work in the evenings. She was a never smoker. We do not have information about the occupation of her parents or close family members (Table 2).

	Case 1	Case 2	Case 3	Case 4
Type of community member	Worker	Resident	Worker	Worker
Smoking	No	No	Yes	Yes
Pack year	0	0	25	1
Marijuana	No	No	No	No
Intravenous/inhaled drugs	No	No	No	No
Dust cloud exposure	No	Yes	No	Yes
WTC ash in home	No	Yes	No	No
Dust in home	No	Light	No	No
Dust duration home	None	more than 1 month	None	None
Cleaned home	No	Yes	No	No
Ingested dust	Yes	Yes	Yes	Yes
Cough dust	Yes	Yes	No	Do not Remember
Work dust	Yes	No	No	Yes
Dust duration work	More than one month	None	None	Unknown
Workplace with ash	Yes	Yes	No	No
Cleaned workplace	Yes	No	No	Yes
Cleaning area	Workplace	Apartment	None	Work place
Cleaning duration (weeks)	13	1	None	Less than one week
Dust in air	Every day or almost everyday	Every day or almost everyday	Unknown	Unknown
Smell lingering	More than 6 months	>3-6 months	more than 6 months	
Appearance	There was no dust in my hair, or on my skin or clothes	My hair, skin and clothing were covered with some dust and debris, and I could brush some of it off before I got home	Not in the dust cloud	My hair, skin and clothing were covered with some dust and debris, and I could brush some of it off before I got home

Dust morning	No	Yes	Yes	Yes
Dust afternoon	No	No	Yes	Yes
Wheezing after 9/11	Yes (12 months)	No	No	No
Cough after 9/11	No	No	No	Mild
Dyspnea with exercise	Yes	Yes	Yes	Yes
WTC EHC: World Trade Center Environmental Health Center				

**Table 2:** Characteristics of WTC related exposure in mesothelioma cases in WTC EHC.

	Case 1	Case 2	Case 3	Case 4
Site	Peritoneum	Peritoneum	Pleura	Pleura
Age at diagnosis	80	38	70	57
Latency from 9/11 (years)	19	15	17	15
Age of death	Not applicable	Not applicable	72	59
Survival (months)	Not applicable	Not applicable	18	21
ICD 10 code	C45.1	C45.1	C45.0	C45.0
Histologic type	Epithelioid mesothelioma	Papillary mesothelioma	Epithelioid mesothelioma	Epithelioid mesothelioma
Grade	Unknown	Well-differentiated	Unknown	Unknown
Stage	Unknown	Unknown	IIIB	IB
Treatment	Unknown	Surgery, Chemotherapy	Chemotherapy	Chemotherapy
Biomarkers				
Positive	WT1, calretinin, D2-40, BER-EP4, mesothelin (95%)	Not available	WT1, calretinin, D2-40, CAM5.2, Ki-67 (40%), CK 5/6, mesothelin (100%)	WT1, calretinin, CAM 5.2, Ki-67 (60%), PDL-1 (15%), CK 5/6, D2-40, CK 7, BER-4, BRG1
Negative	BAP-1, CEA, PDL-1	Not available	BAP1, CEA, PDL-1, BER-EP4, TTF-1, B72.3, p40, HMB-45, S100 protein	BAP1, CEA, MOC31, B72.3, TTF-1, Napsin, Cytokeratin 20, Mucicarmine, MTAP

**Table 3:** The mesothelioma and biomarker profiles of the cases.

## Case 2

A 38-year-old male reported abdominal bloating and intermittent abdominal pain beginning in 2012. An ultrasound of the liver was performed, revealing mild ascites and liver fibrosis. The patient underwent a diagnostic laparoscopy in 2016 for repair of a suspected retroperitoneal/para duodenal hernia. There was no evidence of a retroperitoneal or lesser sac hernia, but there was evidence of significant deposits of mucin on the omentum as well as on the peritoneal surface of the mesentery and some areas in the pelvic peritoneum. These findings were concerning for potential pseudomyxoma appearance. Biopsies were taken of the omentum and the mesenteric surface nodules. The final pathology report of January 2017 from the peritoneal omental and mesenteric biopsies was consistent with well-differentiated papillary mesothelioma. The patient underwent maximal cytoreductive surgery of the peritoneal mesothelioma and hyper thermic intraperitoneal chemotherapy (HIPEC) in January 2017 and tolerated the procedure well. In May 2017, the patient reported having no symptoms related to his treatment or condition. His exam was benign and he continues to be monitored for his condition (Table 1, 3).

The patient had an appendectomy in 2005. He was never a smoker and reported no history of prior asbestos exposure or hobbies with potential dust exposure. We do not know about potential asbestos exposure in close family members. On 9/11/2001, the patient lived several blocks away from the WTC site and did have acute exposure to the WTC dust on 9/11. He was evacuated but returned to his apartment approximately one week after 9/11. He had light dust in his home. He cleaned his home but it was not professionally cleaned. He indicated that the WTC dust had been present in his house for more than 1 month (Table 2).

## Case 3

A 70-year-old male reported left-sided back pain in 2018, which was evaluated with a chest X-ray followed by a chest CT scan. The imaging was abnormal, and pleural biopsy was performed in May 2018 confirming epithelioid malignant mesothelioma of pleura. His biomarker profile was positive for CAM5.2, CK 5/6, Calretinin, WT1 (100%), D2-40, mesothelin (100%) and, Ki-67 (40%) but negative for BAP1, BER-EP4, TTF-1, CEA, B72.3, p40, HMB-45, PDL-1 (<1%) and, S100 protein. The patient received 6 cycles of chemotherapy. Despite treatment, he died 18 months after his diagnosis (Table 1, 3).

The patient had a history of basal cell carcinoma of skin, which was removed in 2017. He reported smoking a pack of cigarettes per day from age 19-46 (26 pack-year). Additionally, the patient reported serving as a member of the U.S. Army for 1 year and 7 months. On 9/11, the patient was working as a sanitation worker at a location nine blocks north of the WTC towers. He

stayed in the area until 10:00 pm when he was able to catch a ferry to Staten Island. He reported exposure to the WTC dust. He returned to work on 9/12 at for 8-hour shifts, 5 days a week, and also reported visiting Ground Zero for multiple sanitation-related visits. He retired in 2008 from the Department of Sanitation (Table 2).

## Case 4

A 57-year-old male presented with a right pleural effusion and right pleural mass (5.0 cm) in 2020. Pleural biopsy was performed in June 2020 confirming epithelioid malignant mesothelioma. The biomarker profile of the patient was positive for calretinin, CK 5/6, WT-1, D2-40, CK 7, BER-4, Cytokeratin CAM 5.2, Ki-67 (60%), PDL-1 (15%) and, BRG1 but negative for BAP1, MOC31, B72.3, CEA, TTF-1, Napsin, Cytokeratin 20, Mucicarmine and, MTAP. He had metastases to the scapula and right femur and a recurrence of mesothelioma in his right thorax. The patient received chemotherapy. Despite treatment, he died 21 months after the diagnosis (Table 1, 3).

The patient smoked cigarettes for 4 years with a one pack/year tobacco history and quit 35 years before his entry into the clinic. On 9/11/2001, the patient was an office worker and did have acute exposure to the WTC dust. He reported his hair, skin, and clothing were covered with some dust and debris. He returned to work 3 weeks after 9/11. His workplace was professionally cleaned (Table 2).

## Discussion

We report 4 cases of mesotheliomas in WTC community members, none of whom were involved in rescue or recovery operations. We report two cases of peritoneal mesotheliomas and two pleural mesotheliomas. All patients reported acute exposure on 9/11/2001, as well as subsequent chronic exposure. We cannot identify other asbestos exposure other than the WTC dust for these patients.

Asbestos is well-reported as a major exposure risk for malignant mesothelioma, originating from the lining cells (mesothelium) of the peritoneal and pleural cavities [15-21]. Asbestos use in the construction of the WTC towers was documented, although limited to part of one building (North Tower). Both chrysotile and amosite asbestos were the most commonly used forms of asbestos for insulation and building construction in the building trades [1-4,8,22,23]. Variable levels of asbestos in the WTC dust in surrounding commercial and residential locations have been described [1,2,3], with highest levels closest to the disaster area. Lioy et al [1] estimated that chrysotile asbestos fibers constituted less than 1% of the volume in samples taken from various streets around the World Trade

Center, mostly bound with a carbonate binder. Documentation of direct asbestos fiber exposure in WTC-exposed individuals is difficult with rare pathologic reports of specimens obtained from the lungs of WTC responders or community members. Chrysotile and amosite asbestos fibers were described in a mineralogic analysis of bronchoalveolar lavage obtained in a firefighter who was exposed heavily to WTC dust [23,24]. Lung biopsies of WTC responders with severe respiratory symptoms or unexplained abnormal radiographic findings revealed an elevated concentration of chrysotile asbestos [25]. A report of lung biopsies in community members with severe respiratory symptoms used a mineralogic method that was unable to detect asbestos fibers [26]. Thus, there is some evidence for presence of inhaled amosite and chrysotile fibers from pathologic specimens from the lungs of responders. There are no data for presence of asbestos fibers in the lungs of community members exposed to WTC dust and fumes from the disaster.

The links between non-occupational asbestos exposure and pleural mesothelioma suggest a significantly elevated risk for both household and neighborhood exposure with fiber-type potency similar to that observed in occupational settings [27,28]. Varied degrees of association with mesothelioma risk were identified based on fiber type, with the strongest links with amphibole and the weakest with chrysotile. Consequently, the types of fibers residents were exposed to may have an impact on mesothelioma rates [27]. Crocidolite and amosite fibers are recognized as the primary causes of mesothelioma among occupationally exposed individuals [29,30].

We report two cases of peritoneal mesothelioma. Peritoneal mesothelioma is usually rare; constituting around 15% - 20% of all mesothelioma cases [31,32], and the second most prevalent form of mesothelioma occurring in the abdomen [33]. The greater intensity of the acute exposure to asbestos is associated with the greater risk for peritoneal mesothelioma [34-37] and affects both genders equally when not caused by occupational exposure [38,39].

Both of our peritoneal mesothelioma patients reported significant WTC dust exposure with potential for asbestos exposure, however their exposures differed. One patient had extensive exposure on 9/11 from the home, the other was a local worker. Both had chronic exposures from living or working in the area. Peritoneal mesothelioma has a shorter latency period from exposure than pleural mesothelioma [20] with an age range typically spanning 40-65 years at diagnosis [38-40] although there is a wide age range [33]. Our two cases of peritoneal mesothelioma had a wide age range at diagnosis; ages 38 and 80, with a relatively short latency from WTC exposure of 15 and 19 years.

Both of the peritoneal mesothelioma patients presented with abdominal pain as their primary symptom. Additional findings for the peritoneal mesothelioma cases included unexplained weight loss, abdominal bloating, and abdominal wall hardening with mild ascites noted on initial examination. These findings are consistent with what has been described for peritoneal mesothelioma cases, in which patients may present with vague and ill-defined signs and symptoms like abdominal pain and ascites [34], and as noted in our cases, diagnosis can often be delayed due to the non-specific presentation of symptoms [41]. The pathologic findings in our two patients also differed. One of our peritoneal mesothelioma cases was diagnosed as well-differentiated papillary mesothelial tumor [33], a distinct and rare subtype of epithelial peritoneal mesothelioma [42], whereas the other was described as epithelioid mesothelioma. Unfortunately, immunohistochemical findings are not available for the patient with well-differentiated papillary mesothelioma as the surgery and treatment were performed at an outside hospital. Although asbestos is a risk for the development of mesothelial malignancy, germline mutations [43] and mutational predisposition may also contribute to risk for peritoneal mesothelioma [33]. We do not have extensive information on mutational risk in our patients with biomarker data available for only one of our patients.

Most mesothelioma cases originate in the pleura [16] as asbestos fibers can reach the pleura through lymphatics or by direct penetration [44] and two of our patients presented with pleural mesothelioma. Both of these pleural mesothelioma cases were exposed as local workers, and both described exposure on 9/11, as well as chronic exposure after the disaster. Both reported a smoking history, although one had a minimal and distant history. One patient had served in the army and we do not have a detailed exposure history from that time. A long latency of pleural mesotheliomas after asbestos exposure has been well-described. The latency period for mesothelioma is highly variable, ranging from 13 to 70 years [45]. This variability is influenced by occupation [46], gender [47], source of exposure [48], as well as the intensity of asbestos exposure and the definition used for latency [49]. Lanphear and Bunker's review [45] of over 1,000 cases report a median of 32 years (1992) with 96% of cases diagnosed at least 20 years after initial exposure and 33% of cases diagnosed 40 years after exposure. Additional studies of exposures to mixed forms of asbestos reported minimum latencies for malignant mesothelioma ranging from 13 to 15 years [46,50-53]. A recent study reported characteristics of 302 pleural mesotheliomas from South America, with a median patient age at diagnosis of 61.1 years [54]. Certification in the WTC Health Program requires a minimum latency of 11 years before a mesothelioma can be labelled as WTC-certified (NIOSH) and our patients were diagnosed with a relatively

short exposure latency of 17 and 15 years respectively. One patient had a short latency (15 years) and an early age of diagnosis (57). Both patients with pleural mesothelioma are deceased. The average age of death from mesothelioma in the United States was 72.8 years according to Surveillance, Epidemiology, and End Results Cancer Registry report between 2009-2015, with a male-to-female (M:F) mortality ratio of 4.2:1, reflecting the historical prevalence of men in asbestos-exposed trades [31,34]. Both pleural mesothelioma patients in our series passed away at ages 72 and 59, with survival periods of 18 and 21 months after diagnosis. Pleural mesotheliomas are generally classified into three subtypes; epithelioid, sarcomatoid, and biphasic, with epithelioid histology presence in 50-70% of cases [55]. Our two pleural mesotheliomas were both described as epithelioid.

Immunohistochemical findings are of increasing importance for diagnosis and management of mesotheliomas. We performed a chart review on all patients to obtain this information, however staining protocols varied, and only incomplete information was available. Various immunohistochemistry biomarkers such as Cam 5.2, calretinin, WT1, D2-40, and others are employed to differentiate the histological subtype of mesothelioma and exclude other carcinomas [16,56-58] and are listed for our cases to differentiate the histological subtype. Hereditary alterations in BRCA1-associated protein 1 (BAP1) and other tumor suppressor genes have been directly linked to mesothelioma, sometimes in conjunction with exposure to asbestos or other carcinogenic fibers [34]. BAP1 functions as a deubiquitylase, regulating the activity of numerous genes and proteins involved in DNA replication, DNA repair, metabolism, and cell death [59,60]. Numerous studies have validated and broadened the understanding of the pathogenic role of BAP1 mutations in mesothelioma and various other cancers [57,61,62]. Additionally, somatically mutated BAP1 (mutations acquired during tumor cell growth) has been detected in approximately 60% of mesotheliomas, highlighting the crucial role of BAP1 in preventing mesothelioma development [63-67]. The biomarker profiles of three patients were available for our review, and none of them exhibited a BAP1 mutation. Programmed death-ligand 1 (PD-L1) was negative in the one peritoneal mesothelioma in which we have data, and was positive in the one pleural mesothelioma with data. PD-L1 is reported as present in 39% of patients and was associated with poorer survival, particularly in non-epithelial mesotheliomas [63,68], and was negative in one of our peritoneal and pleural mesothelioma cases whereas was weak positive in the other pleural case.

## Conclusion

We continue to describe potential health effects from the acute and chronic exposure to the dust and fumes created from the destruction of the WTC towers on 9/11 in the WTC EHC.

Although exposure to asbestos in the building debris was of initial concern, few cases of mesothelioma have been described to date. We report four cases of peritoneal and pleural mesotheliomas in the Survivor (community) population not involved in the rescue and recovery. We were unable to identify an alternative to WTC dust asbestos exposure. Importantly, two of our patients presented at a young age, and all had a relatively short latency from their WTC exposure. Moreover, the presence of two peritoneal malignancies suggests the potential for considerable exposure in these patients. It is imperative to closely watch for additional mesothelioma cases in the WTC-exposed populations to better understand the effects of WTC exposures on the development of this aggressive form of cancer.

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## References

1. Lioy PJ, Weisel CP, Millette JR, Eisenreich S, Vallero D, et al., (2002) Characterization of the dust/smoke aerosol that settled east of the

World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. *Environ Health Perspect* 110: 703-14.

- 2. Landrigan PJ, Liou PJ, Thurston G, Berkowitz G, Chen LC, et al., (2004) Health and environmental consequences of the world trade center disaster. *Environ Health Perspect* 112: 731-9.
- 3. Lippmann M, Cohen MD, Chen LC (2015) Health effects of World Trade Center (WTC) Dust: An unprecedented disaster's inadequate risk management. *Crit Rev Toxicol* 45: 492-530.
- 4. MC Gee Jk, Chen Lc, Cohen Md, Chee Gr, Prophete Cm, et al., (2003) Chemical analysis of World Trade Center fine particulate matter for use in toxicologic assessment. *Environ Health Perspect*, 111: 972-80.
- 5. Allen LP, Baez J, Stern Mec, Takahashi K, George F (2018) Trends and the Economic Effect of Asbestos Bans and Decline in Asbestos Consumption and Production Worldwide. *Int J Environ Res Public Health*, 15: 531
- 6. Nicholson W, Landrigan P (1996) Asbestos: a status report. *Current Issues in Public Health* 2: 118-123.
- 7. Reitze Wb, Nicholson Wj, Holaday Da, Selikoff Ij (1972) Application of sprayed inorganic fiber containing asbestos: occupational health hazards. *Am Ind Hyg Assoc J*, 33: 178-91.
- 8. EPA U (2004) EPA Response to September 11 [Online]. U.S. Environmental Protection Agency.
- 9. Reibman J, Levy-Carrick N, Miles T, Flynn K, Hughes C, et al., (2016) Destruction of the World Trade Center Towers. Lessons Learned from an Environmental Health Disaster. *Ann Am Thorac Soc*, 13: 577-83.
- 10. Program Wt.C. H (2012) Regulations [Online] <https://www.cdc.gov/wtc/conditions.html>
- 11. NIOSH C (2012) Minimum Latency & Types or Categories of Cancer [Online].
- 12. NIOSH, C (2024) World Trade Center Health Program [Online]. <https://www.ecfr.gov/cgi-bin/text-idx?SID=5b2666d4940f00b38d815af01a2e7044&mc=true&node=pt42.1.88&rgn=div5>
- 13. Durmus N, Shao Y, Arslan Aa, Zhang Y, Pehlivan S, et al., (2020) Characteristics of Cancer Patients in the World Trade Center Environmental Health Center. *Int J Environ Res Public Health*, 17: 7190.
- 14. Shao Y, Durmus N, Zhang Y, Pehlivan S, Fernandez-Beros Me, et al., (2021) The Development of a WTC Environmental Health Center Pan-Cancer Database. *Int J Environ Res Public Health*, 18: 1646.
- 15. Bruce Robinson An, Cleo Robinson, Jenette Creaney (2008) Textbook of Lung Cancer, CRC Press.
- 16. Carbone M, Kratzke Ra, Testa Jr (2002) The pathogenesis of mesothelioma. *Semin Oncol*, 29: 2-17.
- 17. Baumann F, Ambrosi Jp, Carbone M (2013) Asbestos is not just asbestos: an unrecognised health hazard. *Lancet Oncol*, 14: 576-8.
- 18. Baur X, Woitowitz Hj, Budnik Lt, Egilman D, Oliver C, et al., (2017) Asbestos, asbestosis, and cancer: The Helsinki criteria for diagnosis and attribution. Critical need for revision of the 2014 update. *Am J Ind Med*, 60: 411-421.
- 19. Elmes P, Browne K (1986) Mesothelioma shortly after brief exposure to asbestos. *Lancet*, 1: 746.
- 20. Frost G (2013) The latency period of mesothelioma among a cohort of British asbestos workers (1978-2005). *Br J Cancer*, 109: 1965-73.
- 21. Goldberg M, Luce D (2009) The health impact of nonoccupational exposure to asbestos: what do we know? *Eur J Cancer Prev*, 18: 489-503.
- 22. Offenberg Jh, Eisenreich Sj, Chen Lc, Cohen Md, Chee G, et al., (2003) Persistent organic pollutants in the dusts that settled across lower Manhattan after September 11, 2001. *Environ Sci Technol*, 37: 502-8.
- 23. Rom WN (2007) Environmental and Occupational Medicine, Lippincott Williams & Wilkins.
- 24. Rom WN, Weiden M, Garcia R, Yie Ta, Vathesatogkit P et al., (2002) Acute eosinophilic pneumonia in a New York City firefighter exposed to World Trade Center dust. *Am J Respir Crit Care Med*, 166: 797-800.
- 25. Wu M, Gordon Re, Herbert R, Padilla M, Moline J, et al., (2010) Case report: Lung disease in World Trade Center responders exposed to dust and smoke: carbon nanotubes found in the lungs of World Trade Center patients and dust samples. *Environ Health Perspect*, 118: 499-504.
- 26. Caplan-Shaw Ce, Yee H, Rogers L, Abraham Jl, Parsia Ss, et al., (2011) Lung pathologic findings in a local residential and working community exposed to World Trade Center dust, gas, and fumes. *J Occup Environ Med*, 53: 981-91.
- 27. Marsh Gm, Riordan As, Keeton Ka, Benson SM (2017) Non-occupational exposure to asbestos and risk of pleural mesothelioma: review and meta-analysis. *Occup Environ Med*, 74: 838-846.
- 28. Xu R, Barg Fk, Emmett Ea, Wiebe Dj, Hwang Wt (2018) Association between mesothelioma and non-occupational asbestos exposure: systematic review and meta-analysis. *Environ Health*, 17: 90.
- 29. Dodson Rf, O'sullivan M, Corn Cj, McLarty Jw, Hammar SP (1997) Analysis of asbestos fiber burden in lung tissue from mesothelioma patients. *Ultrastruct Pathol*, 21: 321-36.
- 30. Sluis-Cremer Gk, Liddell Fd, Logan Wp, Bezuidenhout BN (1992) The mortality of amphibole miners in South Africa, 1946-80. *Br J Ind Med*, 49: 566-75.
- 31. Baumann F Carbone M (2016) Environmental risk of mesothelioma in the United States: An emerging concern,-epidemiological issues. *J Toxicol Environ Health B Crit Rev*, 19: 231-249.
- 32. Mazurek Jm, Syamlal G, Wood Jm, Hendricks Sa, Weston A (2017) Malignant Mesothelioma Mortality - United States, 1999-2015. *MMWR Morb Mortal Wkly Rep*, 66: 214-218.
- 33. Malpica A. (2023) Peritoneal Mesothelioma-An Update. *Adv Anat Pathol*, 30: 262-274.
- 34. Carbone M, Adusumilli Ps, Alexander Hrjr, Baas P, Bardelli F, et al., (2019) Mesothelioma: Scientific clues for prevention, diagnosis, and therapy. *CA Cancer J Clin*, 69: 402-429.
- 35. Chau C, Van Doorn R, Van Poppel Nm, Van Der Stoep N, Mensenkamp AR, et al., (2019) Families with BAP1-Tumor Predisposition Syndrome in The Netherlands: Path to Identification and a Proposal for Genetic Screening Guidelines. *Cancers (Basel)*, 11: 1114.

36. Pavlisko En, Liu B, Green C, Sporn Ta, Roggli VI (2020) Malignant Diffuse Mesothelioma in Women: A Study of 354 Cases. *Am J Surg Pathol*, 44: 293-304.
37. Singhi AD, Krasinskas AM, Choudry HA, Bartlett DL, Pingpank JF, et al. (2016) The prognostic significance of BAP1, NF2, and CDKN2A in malignant peritoneal mesothelioma. *Mod Pathol* 29: 14-24.
38. Lee M, Alexander HR, Burke A (2013) Diffuse mesothelioma of the peritoneum: a pathological study of 64 tumours treated with cytoreductive therapy. *Pathology* 45: 464-73.
39. Liu S, Staats P, Lee M, Alexander HR, Burke AP (2014) Diffuse mesothelioma of the peritoneum: correlation between histological and clinical parameters and survival in 73 patients. *Pathology* 46: 604-9.
40. Alexander HR, Hanna N, Pingpank JF (2007) Clinical results of cytoreduction and HIPEC for malignant peritoneal mesothelioma. *Cancer Treat Res* 134: 343-55.
41. Sharma H, Bell I, Schofield J, Bird G (2011) Primary peritoneal mesothelioma: case series and literature review. *Clin Res Hepatol Gastroenterol* 35: 55-9.
42. Malpica A, Santambrogio S, Deavers MT, Silva EG (2012) Well-differentiated papillary mesothelioma of the female peritoneum: a clinicopathologic study of 26 cases. *Am J Surg Pathol*, 36: 117-27.
43. Panou V, Gadiraju M, Wolin A, Weipert CM, Skarda E, et al. (2018) Frequency of Germline Mutations in Cancer Susceptibility Genes in Malignant Mesothelioma. *J Clin Oncol* 36: 2863-2871.
44. Sterman DH, Albelda SM (2005) Advances in the diagnosis, evaluation, and management of malignant pleural mesothelioma. *Respirology* 10: 266-83.
45. Lanphear BP, Buncher CR (1992) Latent period for malignant mesothelioma of occupational origin. *J Occup Med* 34: 718-21.
46. Bianchi C, Giarelli L, Grandi G, Brollo A, Ramani L, et al. (1997) Latency periods in asbestos-related mesothelioma of the pleura. *Eur J Cancer Prev* 6: 162-6.
47. Haber SE, Haber JM (2011) Malignant mesothelioma: a clinical study of 238 cases. *Ind Health* 49: 166-72.
48. Marinaccio A, Binazzi A, Cauzillo G, Cavone D, Zotti RD, et al. (2007) Analysis of latency time and its determinants in asbestos related malignant mesothelioma cases of the Italian register. *Eur J Cancer*, 43: 2722-8.
49. Peto J, Seidman H, Selikoff IJ (1982) Mesothelioma mortality in asbestos workers: implications for models of carcinogenesis and risk assessment. *Br J Cancer* 45: 124-35.
50. Bianchi C, Bianchi T (2009) Malignant pleural mesothelioma in Italy. *Indian J Occup Environ Med* 13: 80-3.
51. Kamp DW (2009) Asbestos-induced lung diseases: an update. *Transl Res* 153: 143-52.
52. Linton A, Vardy J, Clarke S, Van Zandwijk N (2012) The ticking time-bomb of asbestos: its insidious role in the development of malignant mesothelioma. *Crit Rev Oncol Hematol* 84: 200-12.
53. Selikoff IJ, Hammond EC, Seidman H (1980) Latency of asbestos disease among insulation workers in the United States and Canada. *Cancer* 46: 2736-40.
54. Rojas L, Cardona AF, Trejo-Rosales R, Zatarain-Barrón ZL, Ramírez-Tirado LA, et al. (2019) Characteristics and long-term outcomes of advanced pleural mesothelioma in Latin America (MeSO-CLICaP). *Thorac Cancer* 10: 508-518.
55. Khan AMH, Anwer SH, Sayed S, Mansha MA, Kamran YB, et al. (2023) Comprehensive clinical overview of malignant pleural mesothelioma. *Respir Med* 222: 107511.
56. Carbone M, Guo Z, Mao W (2017) Improving the Accuracy of Mesothelioma Diagnosis in China. *J Thorac Oncol* 12: e132.
57. Carbone M, Kanodia S, Chao A, Miller A, Wali A, et al (2016) Consensus Report of the 2015 Weinman International Conference on Mesothelioma. *J Thorac Oncol* 11: 1246-1262.
58. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, et al. (2015) The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. *J Thorac Oncol* 10: 1243-1260.
59. Dey A, Seshasayee D, Noubade R, French Dm, Liu J, et al (2012) Loss of the tumor suppressor BAP1 causes myeloid transformation. *Science* 337: 1541-6.
60. Yu H, Pak H, Hammond-Martel I, Ghram M, Rodrigue A, et al. (2014) Tumor suppressor and deubiquitinase BAP1 promotes DNA double-strand break repair. *Proc Natl Acad Sci U S A* 111: 285-90.
61. Haugh AM, Njauw CN, Bubley JA, Verzi AE, Zhang B, et al. (2017) Genotypic and Phenotypic Features of BAP1 Cancer Syndrome: A Report of 8 New Families and Review of Cases in the Literature. *JAMA Dermatol* 153: 999-1006.
62. Walpole S, Pritchard AL, Cebulla CM, Pilarski R, Stautberg M, et al. (2018) Comprehensive Study of the Clinical Phenotype of Germline BAP1 Variant-Carrying Families Worldwide. *J Natl Cancer Inst*, 110: 1328-1341.
63. Bueno R, Stawiski EW, Goldstein LD, Durinck S, De Rienzo A, et al. (2016) Comprehensive genomic analysis of malignant pleural mesothelioma identifies recurrent mutations, gene fusions and splicing alterations. *Nat Genet* 48: 407-16.
64. Guo G, Chmielecki J, Goparaju C, Heguy A, Dolgalev I, et al. (2015) Whole-exome sequencing reveals frequent genetic alterations in BAP1, NF2, CDKN2A, and CUL1 in malignant pleural mesothelioma. *Cancer Res* 75: 264-9.
65. Lo Iacono M, Monica V, Righi L, Grosso F, Libener R, et al. (2015) Targeted next-generation sequencing of cancer genes in advanced stage malignant pleural mesothelioma: a retrospective study. *J Thorac Oncol* 10: 492-9.
66. Nasu M, Emi M, Pastorino S, Tanji M, Powers A, et al. (2015) High Incidence of Somatic BAP1 alterations in sporadic malignant mesothelioma. *J Thorac Oncol* 10: 565-76.
67. Yoshikawa Y, Emi M, Hashimoto-Tamaoki T, Ohmura M, Sato A, et al. (2016) High-density array-CGH with targeted NGS unmask multiple noncontiguous minute deletions on chromosome 3p21 in mesothelioma. *Proc Natl Acad Sci USA* 113: 13432-13437.
68. Mansfield AS, Roden AC, Peikert T, Sheinin YM, Harrington SM, et al. (2014) B7-H1 expression in malignant pleural mesothelioma is associated with sarcomatoid histology and poor prognosis. *J Thorac Oncol* 9: 1036-1040.