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# Epidemiologic Study of the Autoimmune Health Effects of a Cargo Aircraft Disaster

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**Background:** In the aftermath of a cargo aircraft crash in Amsterdam in 1992, indications of autoimmune disorders appeared in some of the affected population.

**Methods:** This epidemiologic study sought to determine the possible long-term autoimmune health effects of the aircraft disaster on professional assistance workers. Exposed professional firefighters (n=334) and police officers (n=834) who performed at least 1 disaster-related task and hangar workers who sorted and investigated the wreckage (n=241) were compared with reference groups of nonexposed colleagues who did not perform any disaster-related tasks (n=194, n=634, and n=104, respectively). Data were collected a mean of 8.5 years after the disaster. Questionnaires were used to assess disaster-related tasks and 11 autoimmune-like symptoms. All serum samples were tested for the presence of antinuclear antibodies, rheumatoid factor, and antineutrophil cytoplasmic and anticardiolipin antibodies.

**Results:** Compared with nonexposed colleagues, exposed workers reported significantly more autoimmune-like symptoms. They reported the following symptoms significantly more often: tingling sensations, myalgia, loss of strength, easily fatigued, and a feeling of sand in the eyes (all groups); infection proneness (firefighters); skin abnormalities and nocturnal transpiration (police officers and hangar workers); and vasculitis-like symptoms and Raynaud discoloring (police officers). In contrast, we found no significant difference between exposed and nonexposed workers in autoantibody prevalence.

**Conclusion:** Occupational exposure to the aircraft disaster resulted in an excess of long-term self-reported autoimmune-like symptoms in exposed professional assistance workers, but there was no difference between exposed and nonexposed workers in the prevalence of autoantibodies.

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N OCTOBER 4, 1992, A cargo aircraft crashed into 2 apartment buildings in a densely populated suburb of Amsterdam. The disaster killed 43 people and destroyed 266 apartments. In addition to its sudden impact, an extensive and disturbing aftermath followed the disaster.<sup>1,2</sup> Through the years, media reports suggested various potential health effects and exposures, including exposure to depleted uranium from the balance weights of the aircraft.<sup>3,4</sup> However, in retrospective risk evaluations it was concluded that given the exposure to hazardous materials during the disaster, excess morbidity was unlikely in the people affected by it.<sup>4,5</sup>

In 1998, some cases of autoimmune diseases, and combinations of symptoms that could indicate autoimmunity, came to light in a health inventory of the affected inhabitants and workers. Scientific research has demonstrated the effects of various kinds of

stressors, such as disasters, on the human immune system and its functioning.<sup>7,8</sup> Some of these effects may increase susceptibility to diseases such as autoimmune diseases. In addition, exposure to various xenobiotics, including heavy metals, has been associated with the occurrence of autoimmune reactions, for example, autoantibodies and autoimmune diseases.<sup>9,10</sup>

We aim to assess the long-term autoimmune health effects of occupational exposure to the aircraft disaster as part of the Epidemiological Study Air Disaster in Amsterdam (ESADA).<sup>11</sup> To this end, we investigated whether professional assistance workers exposed to this disaster differ from their nonexposed colleagues with respect to prevalence rates of self-reported autoimmune-like symptoms and autoantibodies.

## **METHODS**

The study protocol of the ESADA has been published previously, 11 but the relevant parts are

described herein. The ESADA can be characterized as a historical cohort study, with self-reported exposure status.

## **PARTICIPANTS**

The study population comprised 3 occupational groups: (1) all (exposed and nonexposed) professional firefighters employed in the Amsterdam fire department on the date of the disaster (additional nonexposed firefighters who started working in this fire department after the disaster were also invited to participate because almost the entire fire department had been exposed to the disaster); (2) all (exposed and nonexposed) police officers employed in the Amsterdam-Amstelland Regional Police Force on the date of the disaster and still employed there on January 1, 2000; and (3) all so-called hangar workers who were registered as working for the departments involved in the transport, security, and sorting of the wreckage on the date of the disaster and who reported that they had been involved in these activities and a random sample of their colleagues, matched for age, sex, department, and job title, who were registered as working for these departments on November 30, 1992, but who did not report that they had been involved in these disasterrelated activities.

A questionnaire assessed occupational exposure to the aircraft disaster regarding various disaster-related tasks, including rescuing people, identifying victims and human remains, firefighting, cleaning up, and sorting the wreckage. We defined workers who reported performing at least 1 disaster-related task as being occupationally exposed and all others as not being occupationally exposed.

#### PROCEDURES AND DATA COLLECTION

The medical ethics committees of both medical centers involved in the ESADA approved the study protocol. All participants signed informed consent forms and participated voluntarily. Data were collected at an outpatient clinic in Amsterdam (the Onze Lieve Vrouwe Gasthuis) and, for approximately half the hangar workers, at Schiphol Airport between January 1, 2000, and March 1, 2002 (a mean of 8.5 years after the disaster). Workers were asked to complete questionnaires assessing, in sequence, disaster exposure, health outcomes, and sociodemographic characteristics. Data from the questionnaires were entered twice, after which inconsistencies were reviewed and mistakes rectified. Trained medical assistants collected blood, urine, and saliva samples from the workers. Blood samples were centrifuged and transported within 2 hours to the Medical Immunology Laboratory at the VU University Medical Center for autoantibody analysis (see "Autoantibodies" section below). The laboratory technicians were unaware of the exposure and health status of the participants. Besides autoantibodies, other laboratory outcomes were assessed, including (differential) leukocyte count, C-reactive protein level, and salivary cortisol concentration.11

#### **AUTOIMMUNE-LIKE SYMPTOMS**

Based on a questionnaire assessing the presence (yes or no) of physical symptoms, we defined 11 symptoms that may occur in patients with autoimmune diseases ("autoimmune-like symptoms"):

 Inflammatory joint or low back pain: current low back pain or pain in other joints for at least 3 consecutive months indicating an inflammatory origin. We defined inflammatory low back pain as low back pain that is most severe at night or when getting out of bed in the morning but not after moving around. For joint pain, we assumed an inflammatory origin if 2 additional conditions were met: the pain was accompanied by stiffness and there was swelling in 1 or more joints for at least 3 consecutive months.

- 2. Skin abnormalities: at least 1 of the following 3 symptoms: strong and sustained oversensitivity of the skin to sunlight, redness in the shape of a butterfly on the nose and cheeks that becomes worse in sunlight, and tightness of the skin in the past 3 months.
- 3. Infection proneness: excessive occurrence of infections or unexplained fever in the past 3 months.
- 4. Vasculitis-like symptom(s): at least 1 of the following 3 symptoms: inflamed (painful) arteries in the past 3 months; (unexplained) small bluish spots (resembling bruises), with or without sores; and numerous oral ulcers for a long time.
  - 5. Tingling sensations: tingling sensations in the past 3 months.
- 6. Nocturnal transpiration: regular and excessive sweating at night during the past 3 months.
- 7. Myalgia: an unusually high level of muscle pain in the past 3 months.
- 8. Loss of strength: an unusual loss of strength in the past 3 months.
- 9. Easily fatigued: being unusually easily fatigued in the past  $3 \, \text{months}$ .
- 10. Feeling of sand in the eyes: feeling of sand in the eyes for a long time.
- 11. Raynaud discoloring: white-blue-red discoloration of the fingers or toes for a long time.

#### **AUTOANTIBODIES**

Serum samples were aliquoted and stored at -30°C until they were analyzed for the presence (defined as positive test results, unless stated otherwise) of autoantibodies by using the following assays:

Antinuclear antibodies of the IgG class: indirect immunofluorescence performed on commercially obtained slides covered with HEp-2 cells (Immuno Concepts, Sacramento, Calif) according to the manufacturer's instructions (serum dilution in a ratio of 1:40); positive test results were characterized by the fluorescence pattern.

Anti–double-stranded DNA antibodies (total immunoglobulin): routine diagnostic procedure using an indirect immunofluorescence technique with *Crithidia luciliae* as substrate<sup>12</sup> and serum samples diluted in a ratio of 1:10; considered only in serum samples with positive, homogeneous antinuclear antibodies.

IgG antibodies against extractable nuclear antigen: enzymelinked immunosorbent assays (ELISAs) (Hycor Biomedical Inc, Garden Grove, Calif) performed according to the manufacturer's instructions; screening was performed using a mixture of 6 antigens, and positive serum samples were subsequently tested using individual ELISAs for SS-A, SS-B, Sm, Sm/RNP, Scl-70, and Jo-1.

IgM rheumatoid factor: routine diagnostic procedure using an ELISA based on heat-aggregated rabbit  $IgG^{13}$ ; rheumatoid factor was considered to be present if the concentration exceeded 20 IU/mL.

Antineutrophil cytoplasmic IgG antibodies against proteinase 3 and against myeloperoxidase: ELISAs (Hycor Biomedical Inc) performed according to the manufacturer's instructions.

IgM and IgG anticardiolipin antibodies: routine diagnostic procedure using an ELISA based on purified cardiolipin; cofactors, such as  $\beta_2$ -glycoprotein I, were provided by a second incubation of the cardiolipin-coated plates with newborn calf serum, and the results were standardized according to the Harris directives. <sup>14,15</sup>

Table 1. Sociodemographic Characteristics of 2499 Exposed, Nonexposed, and Visiting Professional Assistance Workers

	Firefighters		Police Officers		Hangar Workers		
Characteristic	Exposed (n = 334)	Nonexposed (n = 194)	Exposed (n = 834)	Nonexposed (n = 634)	Exposed (n = 241)	Nonexposed (n = 104)	Visitors (n = 158)
Age, mean (SD), y	51.4 (5.9)*	38.8 (9.1)	44.0 (6.2)†	44.8 (7.0)	43.9 (7.8)	43.4 (7.8)	43.5 (7.9)
Sex, %							
M	100	100	88.5	84.9	100	100	100
F	0	0	11.5†	15.1	0	0	0
Level of education, %							
Low	58.7	50.5	20.7	19.7	42.7	44.2	45.6
Medium	27.5	35.1	52.5	51.1	44.4	41.3	40.5
High	6.3	10.3	20.9	23.3	7.5	5.8	7.0
Missing	7.5†	4.1	5.9	5.8	5.4	8.7	7.0
Alcohol consumption, %‡							
None	4.2	12.4	11.4	8.2	10.8	9.6	6.3
Low/moderate	72.8	70.6	74.3	75.7	71.8	67.3	72.8
Excessive	23.1§	17.0	14.3	16.1	17.4	23.1	20.9
Cigarette smoking, %‡							
Never	32.0	44.8	33.1	27.9	34.4	29.8	36.7
Formerly	35.0	29.4	31.7	38.0	31.1	29.8	24.1
Currently	32.9†	25.8	35.3†	34.1	34.4	40.4	39.2
Ethnicity, %‡							
European	100	100	97.2	98.4	96.7	95.2	93.0
Other	0	0	2.8	1.6	3.3	4.8	7.0
Executive function, %‡							
Yes	42.5	20.6	40.3	41.2	34.4	21.2	29.7
No	57.5*	79.4	59.7	58.8	65.6†	78.8	70.3†

<sup>\*</sup>P<.001 by t test for independent groups (age) and Pearson  $\chi^2$  analysis (all others), with nonexposed as the reference group.

## SOCIODEMOGRAPHIC CHARACTERISTICS

Questionnaires assessed the following sociodemographic characteristics of the workers, as described previously<sup>11</sup>: age, sex (male vs female), ethnicity (other/non-European vs European), cigarette smoking (current or former vs never), alcohol consumption (none or light-moderate vs [extremely] excessive), highest level of education completed (low or medium vs high), and executive function (ie, supervising ≥1 workers: yes vs no).

## STATISTICAL ANALYSIS

Sociodemographic characteristics of exposed vs nonexposed workers were analyzed using t tests for independent groups (age) and Pearson  $\chi^2$  analysis (all others). We used logistic (prevalence of autoimmune-like symptoms and autoantibodies) and Poisson (number of autoimmune-like symptoms) regression analyses to compare exposed and nonexposed workers. Besides crude analyses, we adjusted for the previously mentioned sociodemographic characteristics, if applicable. For infection proneness and nocturnal transpiration, we ruled out seasonal effects by adding a dichotomous variable indicating the month of assessment (September through April vs all other months). We regarded 2-sided P<.05 as statistically significant, and we performed Poisson regression analyses using Stata version 7 (Stata Corp, College Station, Tex) and all other analyses using SPSS version 10.1 (SPSS Inc, Chicago, Ill).

## MISSING VALUES

Health outcome data were almost complete (overall, 96.6%; symptoms, 96.9%; and autoantibodies, 99.8%). Workers with miss-

ing values for a particular health outcome were excluded from that specific statistical analysis. To avoid excluding additional workers from adjusted regression analysis, we replaced missing values with median values of each subgroup for sociodemographic characteristics with less than 5% missing values (ie, alcohol consumption, cigarette smoking, ethnicity, and executive function). For level of education (>5% missing values), we added a "missing" category in adjusted regression analyses. Data on age, sex, and season of assessment were complete.

#### **RESULTS**

#### **RESPONSE**

Almost the entire study population could be invited to participate (n=3643 [97%]), and 2564 workers agreed to participate: 71% of the firefighters, 71% of the police officers, and 70% of the hangar workers. As described previously, we included 2499 workers in the statistical analyses: 528 firefighters (63% exposed), 1468 police officers (57% exposed), and 503 hangar workers (48% exposed). The reference group of hangar workers was further subdivided into a nonexposed reference group (21%) and visitors (31%), who reported that they had visited the hangar with the wreckage but had not performed disaster-related tasks. **Table 1** gives the sociodemographic characteristics of all the workers. In general, exposed and nonexposed workers were comparable, with some small, statistically significant, differences. How-

 $<sup>\</sup>uparrow P < .05$  by t test for independent groups (age) and Pearson  $\chi^2$  analysis (all others), with nonexposed as the reference group.

<sup>‡</sup>Missing values (<5%) were replaced by median values within each subgroup.  $\S P < .01$  by Pearson  $\chi^2$  analysis, with nonexposed as the reference group.

Table 2. Autoimmune-like Symptoms Reported by Exposed and Nonexposed Firefighters and Police Officers\*

		Firefigh	nters	Police Officers			
Symptom	Exposed (n = 334)	Nonexposed (n = 194)	Crude and Adjusted ORs or IRRs (95% CIs)	Exposed (n = 834)	Nonexposed (n = 634)	Crude and Adjusted ORs or IRRs (95% CIs)	
Inflammatory joint or low back pain	6.3	6.2	1.0 (0.49-2.1) 0.63 (0.26-1.6)†	8.4	6.9	1.2 (0.83-1.8) 1.2 (0.83-1.8)†	
Skin abnormalities	10.5	3.6	3.1 (1.4-7.2)‡ 2.3 (0.83-6.2)†	13.1	3.6	4.0 (2.5-6.3)§ 4.4 (2.8-7.1)†§	
Infection proneness	4.2	0.5	8.5 (1.1-64.9)   32.3 (2.9-365.0)‡¶	5.9	3.9	1.5 (0.93-2.5) 1.6 (0.95-2.6)#	
Vasculitis-like symptoms	3.6	2.6	1.4 (0.49-4.1) 1.4 (0.34-5.9)†	5.9	1.6	3.9 (2.0-7.8)§ 3.9 (2.0-7.9)†§	
Tingling sensations	14.7	5.7	2.9 (1.5-5.7)‡ 2.5 (1.1-5.7)†	16.2	8.1	2.2 (1.6-3.1)§ 2.3 (1.6-3.2)†§	
Nocturnal transpiration	18.9	9.8	2.1 (1.2-3.7)‡ 1.3 (0.64-2.5)#	19.5	8.5	2.6 (1.9-3.6)§ 2.8 (2.0-3.9)§#	
Myalgia	15.6	1.5	11.7 (3.6-38.0)§ 10.8 (2.9-40.7)†§	11.1	5.8	2.0 (1.3-3.0)‡ 2.1 (1.4-3.1)†§	
Loss of strength	10.6	1.5	7.5 (2.3-24.8)‡ 10.4 (2.5-43.0)†‡	8.8	3.5	2.7 (1.6-4.4)§ 2.8 (1.7-4.5)†§	
Easily fatigued	19.6	6.2	3.7 (1.9-7.0)§ 3.0 (1.4-6.7)†‡	22.8	10.1	2.6 (1.9-3.6)§ 2.7 (2.0-3.7)†§	
Feeling of sand in the eyes	17.1	3.6	5.5 (2.5-12.4)§ 5.2 (2.0-13.9)†‡	13.6	4.9	3.0 (2.0-4.6)§ 3.1 (2.1-4.7)†§	
Raynaud discoloring	2.7	0	NA / · ·	4.0	1.6	2.6 (1.3-5.3)   2.7 (1.3-5.6)†‡	
≥1 Symptom	54.5	23.7	3.9 (2.6-5.7)§ 3.0 (1.8-5.0)†§	54.9	32.0	2.6 (2.1-3.2)§ 2.7 (2.2-3.4)†§	
Symptoms, No., median (IQR)	1.0 (2.0)	0.0	3.0 (2.4-3.8)§ 2.6 (1.9-3.4)†§	1.0 (2.0)	0.0 (1.0)	2.2 (2.0-2.5)§ 2.3 (2.0-2.5)†§	

Abbreviations: CIs, confidence intervals; IQR, interquartile range; IRRs, incidence rate ratios; NA, not applicable owing to the absence of the symptom in nonexposed firefighters; ORs, odds ratios.

ever, exposed firefighters were, on average, more than 10 years older than nonexposed firefighters.

#### **AUTOIMMUNE-LIKE SYMPTOMS**

**Table 2** (firefighters and police officers) and **Table 3** (hangar workers) provide the results regarding autoimmune-like symptoms. Exposed workers and visitors reported 1 or more autoimmune-like symptoms significantly more often than nonexposed colleagues. In addition, exposed workers and visitors reported significantly more autoimmune-like symptoms than their nonexposed colleagues. Compared with their nonexposed colleagues, exposed workers reported the following autoimmune-like symptoms significantly more often: tingling sensations, myalgia, loss of strength, easily fatigued, and a feeling of sand in the eyes (all occupational groups); infection proneness (firefighters); skin abnormalities, and nocturnal transpiration (police officers and hangar workers); and vasculitis-like symptoms and Raynaud discoloring (police officers). Visitors reported

being easily fatigued and skin abnormalities significantly more often than nonexposed hangar workers. In contrast, no difference between exposed or visiting workers and nonexposed workers was found for inflammatory joint or low back pain.

The main complaints of police officers with skin abnormalities, infection proneness, and vasculitis-like symptoms were oversensitivity of the skin to sunlight, excessive occurrence of infections, and (unexplained) bluish spots and numerous oral ulcers, respectively (data not shown). Oversensitivity to sunlight was also the main complaint reported by hangar workers with skin abnormalities.

## **AUTOANTIBODIES**

**Table 4** (firefighters and police officers) and **Table 5** (hangar workers) give the results regarding the autoantibodies. We found no significant difference between exposed or visiting workers and their nonexposed colleagues in the prevalence of autoantibodies. Only 11 workers had IgG antibodies against extractable nuclear

<sup>\*</sup>Data are given as percentage and crude and adjusted ORs for each symptom and for 1 or more symptoms and as median (IQR) and crude and adjusted IRRs for number of symptoms, with nonexposed workers as the reference group.

<sup>†</sup>Adjusted for age, alcohol consumption, cigarette smoking, level of education, executive function, and, for police officers only, sex and ethnicity.

<sup>‡</sup>*P*<.01.

<sup>§</sup>*P*<.001.

<sup>∥</sup>*P*<.05.

<sup>&</sup>quot;Adjusted for season of assessment, age, alcohol consumption, cigarette smoking, and executive function.

<sup>#</sup>Adjusted for season of assessment, age, alcohol consumption, cigarette smoking, level of education, executive function, and, for police officers only, sex and ethnicity.

Table 3. Autoimmune-like Symptoms Reported by Exposed, Nonexposed, and Visiting Hangar Workers\*

		Hangar Workers						
Symptom	Exposed (n = 241)	Nonexposed (n = 104)	Crude and Adjusted ORs or IRRs (95% Cls), Exposed vs Nonexposed	Visitors (n = 158)	Crude and Adjusted ORs or IRRs (95% CIs), Visitors vs Nonexposed			
Inflammatory joint or low back pain	6.7	9.7	0.67 (0.29-1.5)	8.9	0.91 (0.39-2.1)			
			0.67 (0.29-1.6)†		0.97 (0.41-2.3)†			
Skin abnormalities	10.4	1.9	5.9 (1.4-25.3)‡	11.4	6.5 (1.5-28.8)‡			
			6.7 (1.5-28.9)†‡		6.5 (1.5-29.1)†‡			
Infection proneness	5.0	1.0	5.4 (0.70-42.2)	4.4	4.8 (0.58-39.4)			
			5.1 (0.63-40.7)§		4.7 (0.56-38.8)§			
Vasculitis-like symptoms	5.0	0	NA	5.7	NA			
Tingling sensations	18.7	8.7	2.4 (1.1-5.2)‡	14.1	1.7 (0.76-3.9)			
			2.6 (1.2-5.7)†‡		1.7 (0.74-3.9)†			
Nocturnal transpiration	25.8	7.8	4.1 (1.9-9.0)	3.4	1.8 (0.78-4.3)			
			4.8 (2.2-10.8)   ¶		2.0 (0.85-4.9)¶			
Myalgia	24.5	8.7	3.4 (1.6-7.2)#	13.9	1.7 (0.75-3.9)			
			3.6 (1.7-7.7)†#		1.7 (0.73-3.9)†			
Loss of strength	19.5	5.8	4.0 (1.6-9.6)#	7.6	1.3 (0.49-3.7)			
			5.1 (2.0-12.7)†#		1.4 (0.50-4.0)†			
Easily fatigued	36.5	11.5	4.4 (2.3-8.5)	24.7	2.5 (1.2-5.1)‡			
			5.0 (2.5-9.8)†		2.6 (1.3-5.4)†#			
Feeling of sand in the eyes	16.6	6.7	2.8 (1.2-6.4)‡	13.3	2.1 (0.87-5.2)			
			2.7 (1.2-6.3)†‡		2.1 (0.85-5.2)†			
Raynaud discoloring	3.3	2.9	1.2 (0.30-4.4)	2.5	0.88 (0.19-4.0)			
			1.1 (0.29-4.4)**		0.88 (0.19-4.0)**			
≥1 Symptom	61.8	35.6	2.9 (1.8-4.7)	54.4	2.2 (1.3-3.6)#			
			3.1 (1.9-5.1)†		2.2 (1.3-3.7)†#			
Symptoms, No., median (IQR)	1.0 (3.0)	0.0 (1.0)	2.7 (2.1-3.5)	1.0 (2.0)	1.9 (1.4-2.5)			
			2.8 (2.1-3.6)†		1.9 (1.4-2.5)†			

Abbreviations: CIs, confidence intervals; IQR, interquartile range; IRRs, incidence rate ratios; NA, not applicable owing to the absence of the symptom in nonexposed hangar workers; ORs, odds ratios.

antigen, that is, less than 1% in each group. Further subtyping of these 11 workers revealed antibodies against SS-A (n=9), SS-B (n=4), Sm (n=1), Sm/RNP (n=1), Scl-70(n=1), and Jo-1 (n=1) antigens. One of these workers had SS-A, SS-B, and Sm; another had SS-A and Scl-70; and 3 had SS-A and SS-B antigens.

## COMMENT

The results of this study show that, a mean of 8.5 years after the aircraft disaster in Amsterdam, occupationally exposed firefighters, police officers, and hangar workers report more autoimmune-like symptoms than their nonexposed colleagues. However, no difference in autoantibody prevalence was found between exposed and nonexposed workers. The excess prevalence of several autoimmune-like symptoms in exposed workers, particularly of the more specific symptoms, that is, skin abnormalities, vasculitis-like symptoms, and Raynaud discoloring, could indicate a systemic autoimmune or other pathological process. (Auto)immune health effects of psychological stress and certain hazardous materials have also been suggested in other studies. 7-10 However, as mentioned previously herein, we found no significant difference between exposed and nonexposed workers in the prevalence of autoantibodies. Furthermore, the overall prevalence rates of antinuclear antibodies and anticardiolipin autoantibodies in the present study population also resembled those found in other samples of apparently healthy blood donors and the general population. 16-21 It is also unlikely that we found an "earlystage" systemic autoimmune effect, but not yet detected by means of autoantibodies, because of the considerable period between the disaster and the assessment. Moreover, we also found virtually no statistically significant differences between exposed and nonexposed workers regarding the various other hematologic and biochemical clinical outcomes in blood, urine, and saliva (data not shown).11 Thus, we did not find a physiologic basis for the excess in autoimmune-like symptoms among exposed workers. However, we cannot exclude a physiologic but unmeasured basis for these symptoms.

<sup>\*</sup>Data are given as percentage and crude and adjusted ORs for each symptom and for 1 or more symptoms and as median (IQR) and crude and adjusted IRRs for number of symptoms, with nonexposed workers as the reference group.

<sup>†</sup>Adjusted for age, ethnicity, alcohol consumption, cigarette smoking, level of education, and executive function.

<sup>\$</sup>Adjusted for season of assessment, age, ethnicity, level of education, and executive function.

Adjusted for season of assessment, age, ethnicity, alcohol consumption, cigarette smoking, level of education, and executive function.

<sup>\*\*</sup>Adjusted for age, cigarette smoking, and executive function.

Table 4. Autoantibodies in Exposed and Nonexposed Firefighters and Police Officers\*

		Firefighters	<b>:</b>	Police Officers			
Autoantibody	Exposed (n = 334)	Nonexposed (n = 194)	Crude and Adjusted ORs (95% CIs)	Exposed (n = 834)	Nonexposed (n = 633)	Crude and Adjusted ORs (95% Cls)	
ANAs	10.8	6.7	1.7 (0.87-3.3)	10.4	10.3	1.0 (0.73-1.4)	
			1.0 (0.46-2.3)†			1.0 (0.74-1.5)†	
Homogeneous	5.4	0.5	10.9 (1.5-81.9)‡	4.4	4.4	1.0 (0.60-1.6)	
			3.6 (0.45-28.1)§			1.1 (0.66-1.8)†	
Nonhomogeneous	5.4	6.2	0.86 (0.41-1.8)	6.0	5.4	1.1 (0.71-1.8)	
-			0.84 (0.31-2.2)†			1.1 (0.69-1.7)†	
Anti-double-stranded DNA	0.3	0	NA	0.2	0.2	NA	
Anti-ENA	0.6	0.5	NA	0.5	0.3	NA	
RF >20 IU/mL	1.2	1.0	1.2 (0.21-6.4)	0.8	1.0	0.89 (0.30-2.7)	
			0.55 (0.069-4.4)†			0.91 (0.30-2.7)¶	
ANCA PR3	0.3	0.5	NA	0.8	0.6	NA	
ANCA MPO	0	0	NA	0	0	NA	
Anticardiolipin IgG	10.2	7.2	1.5 (0.76-2.8)	6.4	7.6	0.83 (0.55-1.2)	
			1.5 (0.60-3.5)†			0.84 (0.56-1.3)†	
Anticardiolipin IgM	3.9	2.6	1.5 (0.54-4.4)	1.4	2.5	0.56 (0.26-1.2)	
. 3			2.3 (0.53-9.5)§			0.53 (0.25-1.1)†	
≥1 Autoantibody	24.0	17.0	1.5 (0.98-2.4)	18.8	21.3	0.86 (0.66-1.1)	
,			1.3 (0.72-2.3)†			0.87 (0.67-1.1)†	

Abbreviations: ANAs, antinuclear antibodies; ANCA MPO, antineutrophil cytoplasmic IgG antibodies against myeloperoxidase; ANCA PR3, antineutrophil cytoplasmic IgG antibodies against proteinase 3; anti-ENA, IgG antibodies against extractable nuclear antigen; CIs, confidence intervals; NA, not applicable owing to low prevalence; ORs, odds ratios; RF, rheumatoid factor.

Table 5. Autoantibodies in Exposed, Nonexposed, and Visiting Hangar Workers\*

	Hangar Workers							
Autoantibody	Exposed Nonexposed (n = 241) (n = 104)		Crude and Adjusted ORs (95% CIs), Exposed vs Nonexposed	Visitors (n = 158)	Crude and Adjusted ORs (95% Cls), Visitors vs Nonexposed			
ANAs	7.9	10.6	0.72 (0.33-1.6) 0.82 (0.37-1.8)†	9.5	0.89 (0.39-2.0) 0.88 (0.38-2.0)†			
Homogeneous	2.9	5.8	0.49 (0.16-1.5) 0.48 (0.15-1.6)‡	3.8	0.65 (0.20-2.1) 0.55 (0.16-1.9)‡			
Nonhomogeneous	5.0	4.8	1.0 (0.36-3.0) 1.2 (0.40-3.5)†	5.7	1.2 (0.39-3.7) 1.2 (0.39-3.8)†			
Anti-double-stranded DNA§	0	1.0	NA	0	NA			
Anti-ENA	0.4	0	NA	0.6	NA			
RF >20 IU/mL	0.4	0	NA	0	NA			
ANCA PR3	0.4	0	NA	1.3	NA			
ANCA MPO	0	0	NA	0	NA			
Anticardiolipin IgG	5.8	6.7	0.86 (0.34-2.2) 0.89 (0.34-2.3)†	5.7	0.84 (0.30-2.3) 0.91 (0.32-2.6)†			
Anticardiolipin IgM	1.7	3.8	0.42 (0.10-1.7) 0.42 (0.099-1.8)	0.6	0.16 (0.018-1.4) 0.15 (0.016-1.4)			
≥1 Autoantibody	13.7	18.3	0.71 (0.38-1.3) 0.79 (0.42-1.5)†	17.1	0.92 (0.48-1.8) 0.99 (0.51-1.9)†			

Abbreviations: ANAs, antinuclear antibodies; ANCA MPO, antineutrophil cytoplasmic IgG antibodies against myeloperoxidase; ANCA PR3, antineutrophil cytoplasmic IgG antibodies against proteinase 3; anti-ENA, IgG antibodies against extractable nuclear antigen; CIs, confidence intervals; NA, not applicable owing to low prevalence; ORs, odds ratios; RF, rheumatoid factor.

 $\| \text{Adjusted for a} \vec{g} \text{e, alcohol consumption, cigarette smoking, and executive function.}$ 

<sup>\*</sup>Data are given as percentage and crude and adjusted ORs for each individual and for 1 or more autoantibodies, with nonexposed workers as the reference group. †Adjusted for age, alcohol consumption, cigarette smoking, level of education, executive function, and, for police officers only, sex and ethnicity. ‡P<.05.

<sup>§</sup>Adjusted for age, alcohol consumption, cigarette smoking, and executive function.

<sup>||</sup>Anti-double-stranded DNA antibodies were assessed only in cases of homogeneous ANA test results; in all other cases, anti-double-stranded DNA antibodies were assumed to be negative.

<sup>¶</sup>Adjusted for age, sex, alcohol consumption, cigarette smoking, level of education, and executive function.

<sup>\*</sup>Data are given as percentage and crude and adjusted ORs for each individual and for 1 or more autoantibodies, with nonexposed workers as the reference group. †Adjusted for age, ethnicity, alcohol consumption, cigarette smoking, level of education, and executive function.

<sup>‡</sup>Adjusted for age, ethnicity, cigarette smoking, level of education, and executive function.

<sup>§</sup>Anti–double-stranded DNA antibodies were assessed only in cases of homogenous ANA test results; in all other cases, anti–double-stranded DNA antibodies were assumed to be negative.

Posttraumatic stress disorder (PTSD) could also play a role in the assessment of autoimmune health effects of disaster exposure; there is a large body of literature on the co-occurrence of PTSD and adverse physical health outcomes after traumatic events.8 However, adding PTSD symptoms to our multivariate model did not essentially change the effect of exposure. We also found no significant interaction between exposure and PTSD symptoms with respect to the number of autoimmune-like symptoms. Still, irrespective of exposure, the presence of PTSD symptoms was positively and statistically significantly associated with most of the autoimmune-like symptoms (as opposed to the autoantibodies). A (mediating) role of PTSD symptoms in the excess of reported autoimmune-like symptoms in exposed workers is thus probably limited.

Because we found no physiologic basis for and no substantial role of PTSD symptoms in the excess of autoimmune-like symptoms in exposed workers, we may rather deal with a phenomenon commonly described as "unexplained physical symptoms" and "functional somatic syndrome," that is, physical symptoms without sufficient objective, demonstrable pathological abnormalities. This may also reflect a tendency of exposed workers to "overreport" symptoms because they are (unconsciously) more likely to interpret and report bodily sensations as symptoms. Additional reports on individual victims with multiple symptoms that they attributed to the disaster may have amplified this phenomenon.

Unexplained physical symptoms have been described after various other stressful events, particularly when exposure to hazardous materials was feared, such as technological disasters and incidents had war service. After the aircraft disaster, the media reported on various alleged disaster-related exposures, including depleted uranium from the aircraft's balance weights. Therefore, fear of exposure may have also affected symptom reporting by the exposed firefighters and police officers, who mostly performed assistance activities at the disaster site, and the hangar workers, who sorted the wreckage and its balance weights. The prevalence rates of symptoms reported by hangar workers who visited the hangar with the wreckage are mainly in between those of exposed and nonexposed hangar workers.

The methodological strengths of the ESADA are the inclusion of highly comparable reference groups, the fact that almost the entire study population could be invited to participate (97%), the high response rate of 70% of those invited to participate, the considerably large study population, and the completeness and extensiveness of the data. However, some limitations should also be mentioned. One limitation is that only self-reported data on autoimmune-like symptoms are available, with no clinical assessment of these symptoms and their assumed link with autoimmunity. Furthermore, the invitation to the study and assessment of disaster exposure may have affected symptom reporting among exposed workers, particularly if they attributed any symptoms to the disaster. A similar effect on autoantibody prevalence seems unlikely. Thus, we cannot exclude the possibility of overestimating the effect of exposure on symptoms due to such reporting bias. Also, we cannot rule out that exposed workers might have overreported symptoms for reasons of financial compensation. Another methodological weakness is the interval of, on average, 8.5 years between the disaster and the assessment of exposure. Although we cannot exclude recall bias, it seems reasonable to assume that the workers remembered whether they performed any (as opposed to no) disaster-related tasks, which we used to define exposure. Therefore, (non) differential misclassification with respect to exposure is probably limited.

The results of our analysis among the professional fire-fighters are limited by the fact that the nonexposed workers were younger than the exposed firefighters. This was unavoidable because almost the entire fire department was involved in the disaster, so we had to include new nonexposed firefighters who joined this fire department after the disaster. The applied statistical adjustments for age and other potential confounding sociodemographic characteristics may not have fully accounted for this systematic difference between exposed and nonexposed firefighters.

We further acknowledge that we performed multiple statistical tests using P<.05 as a cutoff value for statistical significance. Consequently, it is possible that some of the statistically significant differences between exposed and nonexposed workers are due to chance. However, most of the statistically significant (adjusted) differences between exposed and nonexposed workers have a P<.001, which would most likely also be statistically significant after adjustment for multiple testing. A final limitation concerns the fact that some autoimmune-like symptoms and autoantibodies occurred too rarely to be able to calculate interpretable odds ratios between exposed and nonexposed workers.

In conclusion, the results of this epidemiologic study show that occupational exposure to the 1992 aircraft disaster resulted in an excess of long-term self-reported autoimmune-like symptoms in exposed professional assistance workers but that there is no difference between exposed and nonexposed workers in the prevalence of autoantibodies. These results suggest that disaster workers are at risk for long-term physical symptoms even after 8.5 years and underline the importance of developing optimal aftercare programs for disaster workers after future technological disasters with real and alleged exposure to hazardous materials.

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