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The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED 1812 • ISSN 0028-4793 • WWW.NEJM.ORG

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SOCIETY Volume 329(24), 9 Dec 1993, pp 1760-1763

 About this Journal

 Table of Contents

 Browse TOC

 Find Citing Articles

 Email Jumpstart

 Save Article Text

 Email Article Text

 Print Preview

Links

[Abstract](#)

[Complete Reference](#)

[Catalogo Biblioteca ISS](#)

Outline

- Abstract
- Methods
 - Measurements of Airborne Soybean Allergens
 - Indicators of Asthma
 - Soybean Allergy
 - Statistical Analysis
- Results
- Discussion
- REFERENCES

Graphics

- Figure 1
- Table 1
- Table 2

Recent History

Preventing Asthma Epidemi...



Preventing Asthma Epidemics Due To Soybeans By Dust-Control Measures.

[Original Articles]

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Abstract

Background: The inhalation of soybean dust released during the unloading of soybeans into a silo caused outbreaks of asthma in Barcelona, Spain. This study was designed to determine morbidity due to asthma and serum IgE reactivity before and after the installation of filters in the silo.

Methods: We measured soybean-allergen concentrations in 136 samples of air collected for 9 months before and 24 months after the installation of filters. We compared the number of days on which there was an unexpected increase in emergency room visits for asthma, the number of days on which the number of emergency room visits for asthma in one four-hour period was so high that it was unlikely to be due to chance, and the mean daily number of emergency room and intensive care unit admissions for asthma for a total of 60 months before and after filter installation. Serum IgE antibodies against soybean allergens were measured in 38 patients before and after filter installation.

Results: The concentration of airborne soybean allergens on days when soybeans were unloaded decreased from 324 to 25 U per cubic meter after the installation of filters ($P<0.001$). The number of days on which there was an unusually large number of visits to the hospital for asthma and the number of days on which asthma was epidemic both decreased significantly (both $P<0.001$), from 29 to 6 and from 18 to 0, respectively. The mean daily number of emergency room and intensive care unit admissions for asthma on days when soybeans were unloaded decreased from 8.3 to 5.4 and from 0.26 to 0.01, respectively (both $P<0.001$). The mean serum IgE antibody concentrations in the 38 patients studied decreased from 2 Pharmacia reference units

per milliliter to 1 ($P < 0.001$).

Conclusions: Installing filters on silos to prevent airborne dissemination of allergenic soybean dust eliminates outbreaks of asthma caused by inhalation of the dust, thus supporting the idea that the avoidance of allergens helps prevent asthma. (N Engl J Med 1993;329:1760-3.)

Nearly a decade ago there was a dramatic increase in the number of patients with asthma who were admitted to emergency rooms on specific days in Barcelona, Spain. These outbreaks were characterized by a point-source distribution of cases around the harbor of the city, which suggested that they were due to the inhalation of an environmental agent [1]. Subsequent studies linked the outbreaks of asthma to the inhalation of soybean dust released during the unloading of soybeans into one of the two silos used for storage in the harbor [2,3]. This silo (silo 1) was located close to the center of the city and lacked appropriate filters, with the result that large amounts of soybean dust were released into the air [2]. The other silo (silo 2) was properly fitted with filters. Patients with asthma whose symptoms were exacerbated during these outbreaks had specific serum IgE antibodies that reacted strongly with glycoprotein bands of less than 14.4 kd from soybean extracts [4,5]. The conclusion drawn from these studies was that the outbreaks of asthma were caused by soybean dust [6,7]. Outbreaks of asthma due to the inhalation of soybean dust were subsequently reported in Cartagena, Spain [8-10]. At the beginning of September 1987, the unloading of soybeans into silo 1 in Barcelona was temporarily stopped. Three months later, bag filters were installed at the top of the silo, and the unloading of soybeans was resumed under controlled conditions. We designed this study to assess the changes in various indicators of asthma morbidity and in serum levels of IgE antibodies against soybean antigens after the installation of silo filters.

Methods

Measurements of Airborne Soybean Allergens

Aerosol samples were collected on fiberglass filters for 24 hours with high-volume suction pumps (model CAV-P, MCV, Collbato, Barcelona) located in the urban area where most cases reported during asthma epidemics occurred. A single sample of air was obtained every eight days from January 1987 through September 7, 1987, when silo 1 was used without filters; from September 8, 1987, through December 1987, when unloadings at the silo were canceled; and from January 1988 through December 1989, after the installation of filters on silo 1. The sampling frequency was established before the cause of the outbreaks of asthma had been identified. Air samples were obtained on 136 days, including 34 days when ships were unloaded and 102 when they were not. The fiberglass filters were stored frozen at -20 degreesC until assay, at which time allergens were eluted from the filter sheets and assayed with a radioallergosorbent inhibition test as described by Agarwal et al [\[11\]](#). Reference soybean allergens were prepared as previously described [\[5\]](#).

Indicators of Asthma

The number of days on which there was an unusually large number of emergency room visits for asthma, the number of days on which asthma was considered epidemic, and the number of admissions for asthma to emergency rooms and intensive care units on days when soybeans were unloaded and on days they were not were determined from January 1985 through September 1989. These data were obtained from the emergency room records of the four largest urban hospitals, which accounted for 75 percent of emergency room admissions for asthma in the city [\[12,13\]](#). Since few children were affected during the epidemics of asthma, [\[12\]](#) only patients who were at least 15 years old were studied.

The number of cases of asthma was considered to be unusually large on a given day if the number of emergency room visits for asthma on such a day was so high that the probability that such a number or a higher one was the result of chance was 0.025 or less [2]. This level of probability was calculated by assuming a Poisson distribution, with the 15-day moving average representing the number of cases expected [14]. The number of cases of asthma was considered to have reached epidemic proportions on a given day if the number of emergency room visits for asthma in one four-hour period was so high that it was unlikely to be the result of chance ($P \leq 0.05$). These four-hour clusters were assessed by the Knox and Lancashire approximation [15] of the scan method [16].

Soybean Allergy

To assess the decrease in serum concentrations of IgE antibodies against soybean allergens after the installation of filters, we studied a representative sample of 148 patients who were seen at an emergency room on a day when asthma was considered to be epidemic after the installation of filters. These patients had previously been included in a case-control study, the methods and partial results of which were reported elsewhere [17]. In a study of patients seen during an asthma epidemic before the installation of filters, [3] the prevalence of IgE reactivity against a commercial soybean extract was 74 percent. In addition, we measured IgE antibodies against soybean allergens in serum samples collected from 38 patients during the last epidemic before the filters were installed and two years after filter installation. There were no statistically significant differences in age, sex, place of residence, frequency of atopy, and smoking habits between these 38 patients and the random sample of 148 patients with symptomatic asthma during an asthma epidemic who were studied only after the installation of filters.

Specific IgE antibodies against the commercial soybean antigens were identified by paper radioimmunosorbent assays and radioallergosorbent assays (Pharmacia, Uppsala, Sweden). The results were expressed as a continuous variable with the categorical radioallergosorbent-test scale, in which the values are expressed as the number of Pharmacia reference units (PRUs) per milliliter [3]. Serum samples obtained before the installation of filters were stored at -20 degreesC and then assayed at the same time as the samples obtained after installation.

Cutaneous hypersensitivity to the soybean-allergen preparation was assessed by standard skin-prick tests in 115 patients two years after the installation of filters. The antigens used were obtained from samples of the husks and dust of soybeans unloaded in Barcelona harbor at the time of the previous asthma epidemic. A skin reaction was considered to be positive when the diameter of the resulting wheal was at least 3 mm.

Statistical Analysis

The concentrations of airborne soybean dust, indicators of asthma, and levels of serum IgE antibodies against soybean allergens before and after the installation of filters were compared by two-tailed paired and unpaired t-tests and Fisher's exact probability test. Concentrations of airborne soybean dust and serum IgE antibody concentrations against soybean antigens were normalized by logarithmic transformation. The influence of the proximity of the patient's residence to the soybean point source, a history of occupational exposure to soybeans, the ingestion of foods likely to contain soybeans, age, sex, and serum IgE concentrations on the rate of desensitization to soybean antigens was assessed by logistic-regression modeling [18] (Egret statistical package, Statistics and Epidemiology Research, Seattle).

Results

The concentration of soybean allergens in the air in Barcelona decreased significantly after filters were installed in silo 1 (geometric mean concentrations before and after the installation of filters, 54 and 20 U per cubic meter, respectively; $P < 0.001$). This reduction was due to a marked decrease in the concentration of soybean allergens on days when soybeans were unloaded (geometric mean of 324 U per cubic meter [range, 10 to 10,590] in 12 samples collected before the installation of filters and of 25 U per cubic meter [range, 5 to 165] in 22 samples collected after the installation of filters, $P < 0.001$) [Figure 1](#). There was no significant difference in the concentration on days when soybeans were not unloaded (19 U per cubic meter [range, 9 to 1035] in 18 samples collected before installation, and 18 U per cubic meter [range, 7 to 426] in 84 samples collected after).

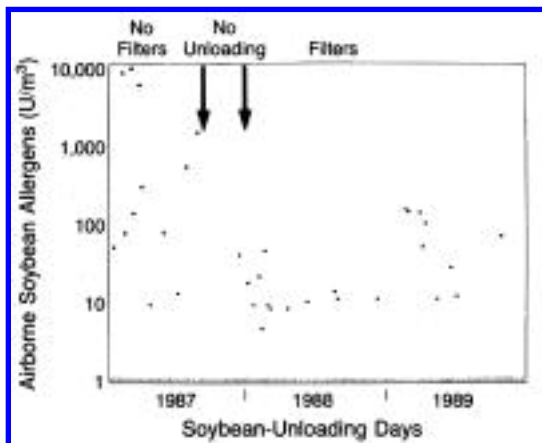


Figure 1.-Concentrations of Airborne Soybean Allergens on Days When Soybeans Were Unloaded in Barcelona before Unloading Was Stopped at Silo 1 (January 1987 through September 7, 1987), during the Period in Which There Was No Unloading (September 8, 1987, through December 1987), and after the Installation of Filters on Silo 1 and the Resumption of Soybean Unloading (January 1988 through December 1989)

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The Y axis has a logarithmic scale *.

There were no days on which asthma was epidemic during the 27 months and 3 weeks

after the installation of filters (defined to include the period when the silo was not used), whereas there were 18 such days during the 32 months and 1 week before the installation of filters ($P<0.001$) [Table 1](#). The number of days on which there was an unusually large number of emergency room visits for asthma also decreased significantly (from 29 to 6) after the filters were installed ($P<0.001$). Again, the decrease occurred only when soybeans were unloaded; there was no change or a trend in the opposite direction on days when soybeans were not unloaded. The most striking difference was in the number of admissions for asthma to intensive care units on days when soybeans were unloaded, with a mean daily decrease from 0.26 to 0.01 ($P<0.001$) [Table 1](#), although there was also a statistically significant decrease in admissions to intensive care units on days on which soybeans were not unloaded.

Variable	Total Days	Days when Unusually Large No. of Asthma Cases	Days on which Soybean Was Unloaded	Emergency Room no. of admissions	Intensive Care Unit
Unloading					
Before filter installation	167	29	18	8.3±11.1	0.26±0.90
After filter installation	130	6	11	5.4±3.0*	0.01±0.12†
No unloading					
Before filter installation	815	11	2	4.7±2.2	0.04±0.08
After filter installation	711	12	8	3.0±2.3	0.01±0.11‡

*Data are for 1981 to 1991. Plus-minus values are means ±SD.
† $P<0.001$ for the comparison with values obtained before filter installation on days on which soybeans were unloaded.
‡ $P = 0.008$ for the comparison with values obtained before filter installation on days on which soybeans were not unloaded.

Table 1. Indicators of Asthma before and after the Installation of Filters, According to Whether Soybeans Were or Were Not Being Unloaded

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The installation of filters also affected other indicators of asthma on days when soybeans were unloaded. The mean number of admissions for asthma to emergency rooms on days when soybeans were unloaded dropped from 8.3 to 5.4 per day ($P<0.001$). The difference between these two means multiplied by the number of days when soybeans were unloaded after the installation of filters is 386 -- the number of emergency room admissions for asthma prevented by the installation of filters. The number of emergency room admissions for asthma on days when soybeans were unloaded decreased in all age and sex categories, with the decrease being greatest

among men over 45 years of age [Table 2](#). In contrast, there was a small increase in emergency room admissions for asthma among young adults of both sexes on days when soybeans were not unloaded.

AGE (YR)	SOYBEAN UNLOADING			NO SOYBEAN UNLOADING		
	BEFORE FILTER INSTALLA- TION	AFTER FILTER INSTALLA- TION	P VALUE	BEFORE FILTER INSTALLA- TION	AFTER FILTER INSTALLA- TION	P VALUE
	no. of admissions/day			no. of admissions/day		
Men						
15-44	1.1±0.9	0.8±0.9	NS	0.7±0.9	0.8±0.9	0.04
45-64	1.5±2.5	0.6±0.8	<0.001	0.6±0.8	0.6±0.8	NS
>64	0.8±1.8	0.3±0.5	0.003	0.3±0.6	0.3±0.6	NS
Women						
15-44	1.5±2.1	1.2±1.1	NS	1.0±1.0	1.3±1.1	<0.001
45-64	1.9±2.7	1.3±1.2	0.007	1.2±1.2	1.1±1.0	NS
>64	1.3±1.7	1.0±1.0	NS	0.8±0.9	0.8±1.0	NS

Table 2. Daily Emergency Room Admissions before and after the Installation of Filters, According to Age and Sex and According to Whether Soybeans Were or Were Not Being Unloaded

*Data are for 1985 to 1990. Plus-minus values are means ±SD. NS denotes not significant.

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With respect to soybean allergy, the prevalence of serum IgE reactivity with commercially prepared soybean extract in a previous study conducted before the installation of filters was 74 percent [\[3\]](#). Among the 148 patients seen during an asthma epidemic after the installation of filters, 77 (52 percent) had measurable serum concentrations of specific IgE antibodies against soybean allergens. Sixty (52 percent) of the 115 patients seen during an asthma epidemic in whom skin tests were performed had positive reactions to the local soybean-husk allergen, and 50 (43 percent) had positive reactions to the local soybean-dust allergen.

Of the 38 patients seen during an asthma epidemic for whom serum samples had been obtained before and after the installation of filters, 29 (76 percent) had measurable concentrations of IgE antibodies against soybean allergens two years after the installation of filters, as compared with 32 (84 percent) before the installation of filters. The mean serum concentration of IgE antibodies against soybean allergens in these 38

patients decreased from 2 PRU per milliliter before the installation of filters to 1 PRU per milliliter afterward ($P < 0.001$). When the results of the radioallergosorbent test were expressed semiquantitatively, 18 patients had a decrease in specific IgE antibodies after the installation of filters, whereas 2 patients had an increase ($P = 0.006$). The rate of the decrease in the serum concentrations of IgE antibodies against soybean allergens was not related to the proximity of the patient's residence to the soybean point source, a history of occupational exposure to soybeans, the ingestion of foods likely to contain soybeans, age, sex, or serum IgE concentrations.

Discussion

The installation of filters in a particular silo in Barcelona harbor was very effective in reducing the amount of soybean dust in the air and in preventing subsequent outbreaks of asthma. Not only did outbreaks no longer occur, but the number of days on which there was an unusually large number of cases of asthma also decreased. In previous studies by our group, [2-4] epidemiologic criteria for a causal relation between the unloading of soybeans and epidemics of asthma were fulfilled, except for a dose-response relation, but evidence of the effect of filter installation was still preliminary [6]. The cessation of epidemics of asthma after the installation of filters provides strong confirmation of such a causal relation.

The results of this study also demonstrate the impact of the installation of filters on other indicators of asthma. Two aspects deserve special consideration. First, the most marked reduction in the mean number of emergency room admissions for asthma on days when soybeans were unloaded occurred among men over 45 years of age. According to our estimates, this group would have accounted for 48 percent of the emergency room admissions for asthma that would have occurred from October 1987 through December 1989 had filters not been installed in silo 1. This finding is

consistent with that of a previous study, [17] which demonstrated that older men with asthma in Barcelona were more susceptible to epidemics of asthma, and confirms one of the most striking features of asthma epidemics due to soybean dust: older subjects have the highest rates of asthma attacks.

Second, there was a substantial reduction in the number of admissions for asthma to intensive care units. The rate of admissions on days soybeans were unloaded dropped from 26 per 100 days to 1 per 100 days after the installation of filters, so that admissions for asthma to intensive care units have become rare in Barcelona (2.1 admissions for asthma per million inhabitants per year). In a previous study, [19] we found that most of the critically ill patients hospitalized during days on which asthma was epidemic had an abruptly occurring asthma attack followed by rapid relief of symptoms after conventional treatment in the intensive care unit. A similar course of illness was reported by Wasserfallen et al\ [20] and O'Hollaren et al., [21] suggesting that the severe attacks are caused by massive exposure to an inhaled allergen. However, the causal evidence in these later studies was mostly circumstantial [22]. In contrast, we found a clear causal link between the inhalation of an aeroallergen -- soybean dust -- and the occurrence of life-threatening asthma. The results also demonstrate that the identification of the source of an allergen and the avoidance of exposure to it can play a substantial part in the prevention of severe, acute asthma. Before the installation of filters in Barcelona, at least 26 people died during the outbreaks with symptoms consistent with those of an asthma crisis.

We found that serum IgE antibodies against soybean allergens persisted for two years after the installation of filters and the cessation of epidemics of asthma. The actual duration of the persistence of serum IgE antibodies could be even longer if our analysis

was biased by regression toward the mean. This possibility cannot be excluded, since the results were based on a single preintervention measure. This relatively high residual level of sensitization to soybean allergens two years after the installation of filters is consistent with the results of other studies on occupational [23-25] and nonoccupational [26,27] asthma. The persistence of serum IgE antibodies and skin reactivity to soybean allergens after a long period of avoidance of exposure could be a result of the retention of the allergen in the lung or extrapulmonary tissue or of the autonomous production of IgE by B cells, as has been suggested by Venables et al [23]. However, persistent exposure to the background levels of soybean allergen in the air in Barcelona after the installation of filters could also explain the continuing sensitization.

Although evidence derived from studies of asthma epidemics cannot be directly extrapolated to cases of asthma that occur at other times, we conclude that more attention should be paid to the primary prevention of asthma through the precise identification of causative allergens and the subsequent avoidance of exposure to these allergens.

We are indebted to Carlos Murillo, Ph.D., Prof. A.J. Newman Taylor, and Francisco X. Real, M.D., for their valuable scientific advice; to the members of the Barcelona Asthma Collaborative Group, who participated in various aspects of this study; to Ms. Helena Martinez for assistance in the preparation of the manuscript; and to Marta Pulido, M.D., for editing the manuscript.

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Figure 1

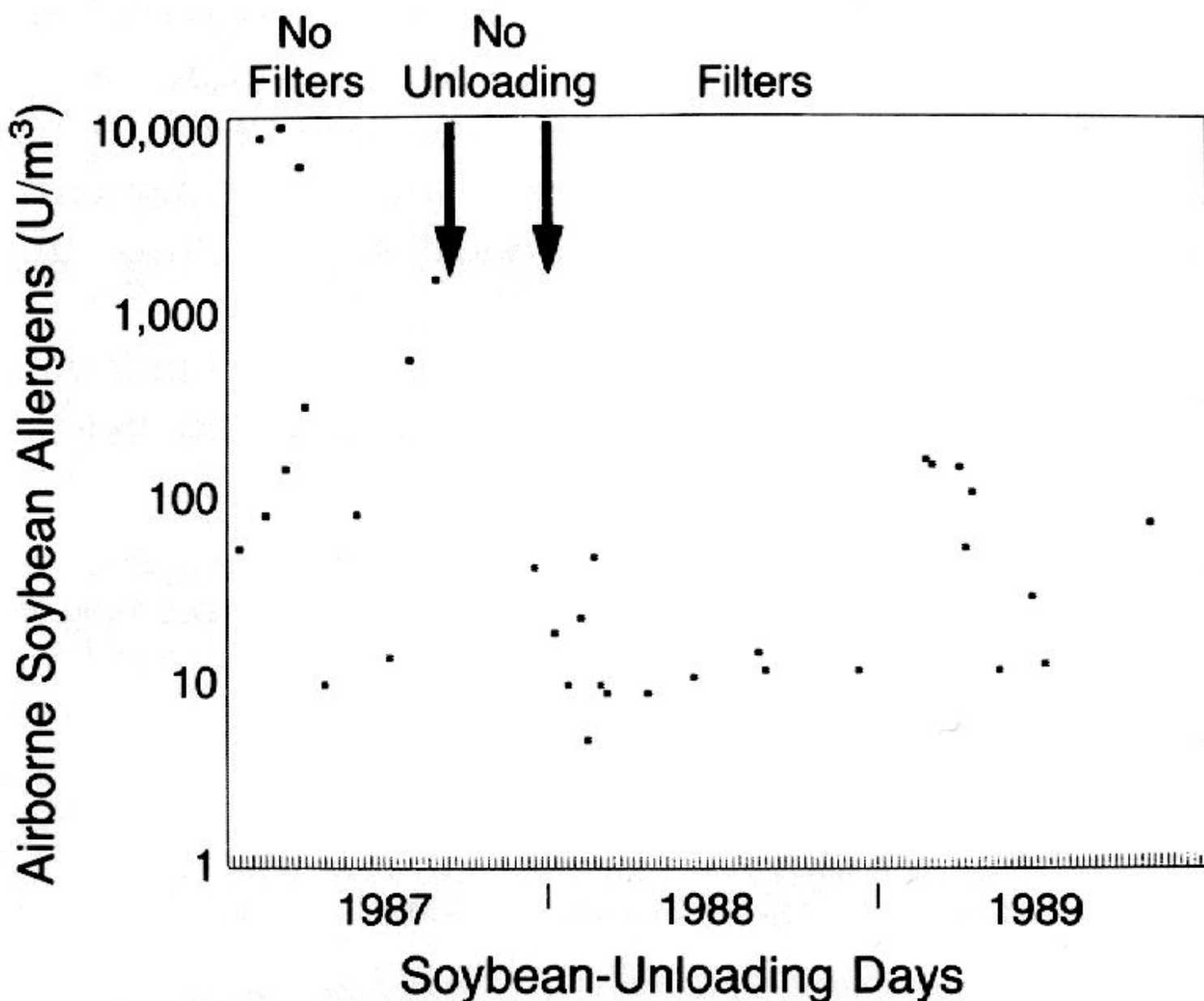


Figure 1. -Concentrations of Airborne Soybean Allergens on Days When Soybeans Were Unloaded in Barcelona before Unloading Was Stopped at Silo 1 (January 1987 through September 7, 1987), during the Period in Which There Was No Unloading (September 8, 1987, through December 1987), and after the Installation of Filters on Silo 1 and the Resumption of Soybean Unloading (January 1988 through December 1989)

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Table 1

VARIABLE	TOTAL DAYS	DAYS WITH UNUSUALLY LARGE NOS. OF ASTHMA CASES	DAYS ON WHICH ASTHMA WAS EPIDEMIC	EMERGENCY ROOM	INTENSIVE CARE UNIT
				<i>no. of admissions/day</i>	
Unloading					
Before filter installation	167	29	18	8.3±11.1	0.26±0.90
After filter installation	133	6†	0†	5.4±3.0†	0.01±0.12†
No unloading					
Before filter installation	815	11	1	4.7±2.5	0.04±0.19
After filter installation	711	12	0	5.0±2.5	0.01±0.11‡

*Data are for 1985 to 1991. Plus-minus values are means ±SD.

†P<0.001 for the comparison with values obtained before filter installation on days on which soybeans were unloaded.

‡P = 0.008 for the comparison with values obtained before filter installation on days on which soybeans were not unloaded.

Table 1. Indicators of Asthma before and after the Installation of Filters, According to Whether Soybeans Were or Were Not Being Unloaded
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Table 2

AGE (YR)	SOYBEAN UNLOADING			NO SOYBEAN UNLOADING		
	BEFORE FILTER INSTALLA- TION	AFTER FILTER INSTALLA- TION	P VALUE	BEFORE FILTER INSTALLA- TION	AFTER FILTER INSTALLA- TION	P VALUE
	<i>no. of admissions/day</i>			<i>no. of admissions/day</i>		
Men						
15-44	1.1±0.9	0.8±0.9	NS	0.7±0.9	0.8±0.9	0.04
45-64	1.5±2.5	0.6±0.8	<0.001	0.6±0.8	0.6±0.8	NS
>64	0.8±1.8	0.3±0.5	0.003	0.3±0.6	0.3±0.6	NS
Women						
15-44	1.5±2.1	1.2±1.1	NS	1.0±1.0	1.2±1.1	<0.001
45-64	1.9±2.7	1.3±1.2	0.007	1.2±1.2	1.1±1.0	NS
>64	1.3±1.7	1.0±1.0	NS	0.8±0.9	0.8±1.0	NS

*Data are for 1985 to 1991. Plus-minus values are means ±SD. NS denotes not significant.

Table 2. Daily Emergency Room Admissions before and after the Installation of Filters, According to Age and Sex and According to Whether Soybeans Were or Were Not Being Unloaded
 From: Anto: N Engl J Med, Volume 329(24).Dec 9, 1993.1760-1763