Daily changes of peak expiratory flow and respiratory symptom occurrence around a soy processing factory

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INTRODUCTION

The influence of exposure to organic matter, emitted by different sources into the ambient air of relatively densely populated areas has been studied in a number of situations. Early studies conducted in the USA [1], South Africa [2] and Brazil [3] around castor bean processing factories showed that dust exposure was positively associated with the occurrence of positive skin prick tests to castor beans and with the development of asthma attacks, either naturally or experimentally. These observations are supported by findings from occupational settings where soy sensitization is highly prevalent among soy allergen exposed workers [4–8].

Outbreaks of asthma exacerbations in the Spanish city of Barcelona have been found to be positively associated with the unloading of soy beans using a large harbour silo without bag filters on top. In total, 26 outbreaks of asthma have been described between 1981 – 1988 causing an excess of 1,155 emergency room admissions among 687 persons without bag filters on top. In total, 26 outbreaks of asthma exacerbations in the Spanish city of Barcelona have been described between 1981 – 1988 causing an excess of 1,155 emergency room admissions among 687 persons.

METHODS

Situation. The oil-producing factory has been situated in Utrecht since 1908, a city in the centre of The Netherlands. Before 1974, production consisted mainly of linseed oil. Since the 1990s, and up to the time of this study, only soybean oil...
was being produced. Soybeans were delivered to the factory by ship via the Amsterdam-Rijn canal. The produced soybean oil was also transported by ship. Soy scrap, which remained after extraction, was removed by trucks. The production process made use of cyclo-hexane extraction, and as a result, the remaining soy scrap was very dry and dusty. Unloading of soybeans from ships on the canal adjacent to the factory was carried out without dust reducing technology and caused visible dust emissions. Loading ships with soybean oil did not cause any problems of this nature. Loading trucks with soy scrap also caused dust clouds around the factory area. The factory operated continuously throughout the day and night. Once a week, the unloading of soybeans was stopped, to load the oil. Loading of oil took place at exactly the same location on the canal. The transport route of the trucks ran through the surrounding neighbourhood. Soy scrap regularly fell off the trucks, and this may have contributed to residential soybean dust exposure. The factory was surrounded by two residential areas, 'Oog in Al' on the west side, and 'Lombok' on the east side. Complaints of residents in the area mostly dealt with the odour emitted by the factory and the trucks running straight through their neighbourhood.

Selection of subjects and measurement of health parameters.

Short questionnaires on allergies and respiratory symptoms were sent to a random sample of 1,000 subjects in the two quarters surrounding the factory (exposed area) and to 1,000 subjects in two quarters located on the other side of the same town, 4 – 5 km from the factory (control area). These random samples were obtained through the municipal registries. Subjects who reported a doctor-diagnosed allergy to house dust, pets and/or pollen or doctor diagnosed asthma were selected for subsequent evaluation. Invited subjects filled out a detailed questionnaire on respiratory symptoms, smoking habits, work-related exposure and home characteristics. Skin prick tests (SPT) to house dust mite, trees, grasses, moulds, cat, dog (ALK-Benelux, The Netherlands) and soy (ALK-Benelux, The Netherlands, Product No. SQ57.06; Lot No. 94K24–0200) were performed in selected individuals.

PEF was measured 3 times in the morning and 3 times in the evening, using a Mini-Wright Peak Flow Meter. The highest of 3 measurements at the same moment was used in further analyses. Respiratory symptoms used in the analyses were 'lower respiratory symptoms' (question on wheezing and/or question on shortness of breath and/or question on attacks of shortness of breath with wheezing positive), 'upper respiratory symptoms' (question on runny or stuffed nose and/or question on sore throat positive) an 'cough' (question on cough and/or question on cough with phlegm positive). Bronchodilator use (in this study only Ventolin, Brycanyl and/or question on sore throat positive) an 'cough' (question on respiratory symptoms directly after exposure, and 1, 2 and 3 hours after exposure (time lags of 0, 1, 2 and 3 days). Days with reports of fever were excluded from all analyses to account for days with respiratory infections.

Differences in PEF were analyzed using linear auto-correlation, adjusting for day of the week (weekend days opposed to weekdays), linear trend and the minimum temperature 2 days before measurement of the PEF. This was done because the minimum temperature 2 days before measurement of the PEF had the strongest influence in the expected direction, i.e. colder days showed a lower PEF. Individual results were combined using linear regression analysis, with the individual difference (L/min) in PEF between exposed days and unexposed days as dependent variable and skin prick test positivity to soy, age, gender, and smoking as independent
variables. Unfortunately, some subjects had been exposed for only a small number of days, resulting in poor estimation of the difference in PEF between days with and days without exposure; therefore, only subjects with more than 3 days exposure were included in further analyses. All subjects with a positive skin prick test to soy had been exposed for more than 3 days. For analysis of the day-to-day changes in reported respiratory symptoms (i.e. ‘Lower respiratory symptoms’, ‘Upper respiratory symptoms’ and ‘Cough’) and bronchodilator use, the individual difference (%) between the prevalence of a symptom on exposed days and the prevalence of a symptom on unexposed days was calculated. Again linear regression analysis was used with the same independent variables as used in the PEF analyses.

Measurements of dust, soybean allergens and endotoxin were also compared to the wind direction with regard to the factory. The samples were allocated into 3 groups, depending on the length of the period the sampling location had been ‘exposed’. In these analyses, also an angle of 90° was used as cut-off point in determining exposure of the measuring location. When a sample had not been exposed during sampling time it was placed in the category ‘not exposed’, when it had been exposed for less than half of the time it was placed in the category ‘partly exposed’, and when it had been exposed for half of the time or more (usually 5 hours or more) it was placed in the category ‘exposed’.

RESULTS

Among the 2,000 individuals asked to fill-in a screening questionnaire, the response rate was 18.9% and a total 108 persons were asked to participate. These individuals had responded to the questionnaire that they had an allergy or were ever diagnosed with asthma. Of these, 53 subjects from the exposed area and 30 subjects from the control area participated. A total of 46 subjects in the exposed area participated in skin prick testing (of those who refused, 2 had recently undergone skin prick testing in a clinic). Skin prick testing was performed in 26 of the subjects in the control area. Histamine was used as positive control tests and the negative control test did not show a reaction in any of the tested subjects. Wheal size diameters of 3 mm after 15 minutes were regarded as positive. For soy, all visible (which in this study means larger than 1.8 mm) wheals were regarded as positive. Daily records of respiratory symptoms and PEF were kept by 51 subjects in the exposed area and 30 subjects in the control area for about 10 weeks from October – December. The samples were allocated into 3 groups, depending on the length of the period the sampling location had been ‘exposed’. In these analyses, also an angle of 90° was used as cut-off point in determining exposure of the measuring location. When a sample had not been exposed during sampling time it was placed in the category ‘not exposed’, when it had been exposed for less than half of the time it was placed in the category ‘partly exposed’, and when it had been exposed for half of the time or more (usually 5 hours or more) it was placed in the category ‘exposed’.

Table 1 shows the difference in PEF between days with and days without exposure, decreasing gradually. A 25 L/min difference between days corresponds to a decrease in PEF of about 5% in this small sample of soy positive subjects. No significant changes occurred in the results when analyses were adjusted for age, gender and smoking, or average daily temperature.

Table 3 shows the difference in prevalence of reports of respiratory symptoms and of the use of bronchodilators between days when the home was downwind from the factory, as opposed to days when the home was upwind. For the morning PEF, lower values were found, especially 1 – 2 days after a downwind day. For the evening PEF, this difference was most pronounced directly after exposure, decreasing gradually. A 25 L/min difference between days corresponds to a decrease in PEF of about 5% in this small sample of soy positive subjects. No significant changes occurred in the results when analyses were adjusted for age, gender and smoking, or average daily temperature.

Table 2 shows the results of the multiple regression analyses with the difference in morning and evening PEF as dependent variables. In this Table, the differences are shown for individuals with a negative skin prick test and a positive skin prick test to soy separately. The differences are shown for the area surrounding the factory and the control area separately, and for a possibly delayed reaction to exposure by applying different time lags. For the morning PEF, as well as for the evening PEF, no statistically significant differences in the expected direction were found for individuals living in the control area. Individuals living in the area surrounding the factory with a positive skin prick test to soy had a statistically significantly lower PEF on days when the home was downwind from the factory, as opposed to days when the home was upwind. For the morning PEF, lower values were found, especially 1 – 2 days after a downwind day. For the evening PEF, this difference was most pronounced directly after exposure, decreasing gradually. A 25 L/min difference between days corresponds to a decrease in PEF of about 5% in this small sample of soy positive subjects. No significant changes occurred in the results when analyses were adjusted for age, gender and smoking, or average daily temperature.

Table 3 shows the difference in prevalence of reports of respiratory symptoms and of the use of bronchodilators between days when the home was downwind and upwind from the factory. In the area surrounding the factory the
premises of the factory were clearly elevated (GM 365 μg/m³ (n=4; GSD 2.5). However, levels were not associated with wind direction and could not be associated with soy dust emissions by the factory, apart from the measurements on the factory premises. Figure 1 shows that for the measurements in the control area, one out of 12 samples contained soy allergens in detectable quantities (>limit of detection (LOD))(1/12=8.3%)). Samples from location A in the area surrounding the factory contained detectable quantities of soy allergen more often when exposed (6/23=26%). The soy allergen content of samples from location B, however, was not clearly associated with exposure by wind from the direction of the factory. Location B was situated in the vicinity of the transport route of soy scrap. All samples taken on the factory premises contained relatively large quantities of soy allergen (all samples positive: 100% detectable). Some additional floor dust samples were taken by using a vacuum cleaner and vacuuming a square meter of street surface from the streets. On the streets, soy was detected in all but one sample (n=7).

**Table 3.** Mean difference(%) (95% confidence interval) in bronchodilator use (A), lower respiratory symptoms (B), upper respiratory symptoms (C) and cough (D), in subjects with negative (soy SPT-) and subjects with positive (soy SPT+) skin prick test to soy, between days with and days without exposure

### A: Bronchodilator use

<table>
<thead>
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<th>Lag (days)</th>
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<th>Control area n=26</th>
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<td>4.6 (1.1;10.3)</td>
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<td>4.2 (-1.3;9.7)</td>
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<td>7.7 (12;14.2)</td>
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### B: Lower respiratory symptoms

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<td>2.5 (-4.6;11.1)</td>
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<tr>
<td>1</td>
<td>1.3 (-4.6;2.0)</td>
<td>3.8 (-4.4;12.0)</td>
</tr>
<tr>
<td>2</td>
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<td>8.3 (-0.3;16.9)</td>
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<tr>
<td>3</td>
<td>-0.4 (-3.9;3.1)</td>
<td>7.9 (-0.5;16.3)</td>
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### C: Upper respiratory symptoms

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<td>15.6 (-4.8;36.0)</td>
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### D: Cough

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<td>1.7 (-15.4;12.0)</td>
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<tr>
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<td>1.7 (-3.0;9.2)</td>
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<td>4.9 (-19.2;10.4)</td>
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<tr>
<td>3</td>
<td>1.1 (-5.6;7.8)</td>
<td>-3.4 (-20.4;13.6)</td>
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</table>

**Figure 1.** Soy allergen concentrations in control area, area surrounding the factory and outside on factory premises. A – sampling location north of factory. B – sampling location southeast of factory in the vicinity of soy scrap transport route. The number of samples with undetectable soy allergen concentrations are shown (# samples—limit of detection)

**Figure 2.** Shows airborne endotoxin concentrations at the 4 sampling locations. Samples from the factory premises...
DISCUSSION

The results of this panel study of susceptible individuals living in the vicinity of a soy processing factory show that acute changes in daily recorded PEF and reports of respiratory symptoms and the use of bronchodilators by soy sensitized individuals are possibly associated with exposure to dust from this factory. Individuals chosen for the presented study were selected by questionnaire. Only about 11% of the selected individuals had a positive skin prick test to soy, which is comparable to 6.5% soy bean positive skin prick tests among atopic French agricultural workers [6], and less than the percentages positive reactors [19 – 39 among asthmatic bakery workers [7, 8]. No data are available for more comparable groups of subjects. No difference was seen for soy-sensitization between the area surrounding the factory and the control area. Although comparison of the 2 areas was not the main aim of the study, and could be hampered by selection bias, it seems that sensitization to soy does not seem to occur very often among susceptible individuals living around the factory. All individuals with a positive skin prick test to soy also showed a positive skin prick test to one or more of the common allergens.

In this study, the exposure of each individual had to be considered separately, day-by-day, because of the nature of the source and the study subjects living randomly around the factory. It was not possible to take dust samples each day for each individual. Therefore, the prevailing wind direction with regard to the position of the factory was used to construct a daily exposure variable for each person. Although samples taken downwind contained soy allergen significantly more often than samples not taken downwind, the measurements of soy allergen also showed that in the quarters through which the soy scrap is transported, some samples also contained soy allergen when the wind had not been from the direction of the factory at all. A possible explanation for this phenomenon could be that soy scrap is lost frequently by the passing trucks, contributing to exposure along the truck route also on days when the wind was not from the factory. This may have resulted in some exposure misclassification leading to an underestimation of the effect.

Considering that acute effects are only seen among individuals with a positive skin prick test to soy an IgE mediated mechanism is expected. Effects on morning PEF and reports of respiratory symptoms, however, were not limited to the day directly after exposure. Effects 2 – 3 days after exposure could be related to airway inflammation, as is often seen in panel studies on community air pollution.

Individuals living in the area near the soy factory are more frequently exposed to detectable levels of soy allergens in the air than individuals living in the control area. Moreover, overall contamination of the environment (soy shed on streets from truck transport) and re-suspension of soy containing dust on the streets is likely to contribute to soy exposure in the area in the vicinity of the factory. The partly exposed area did not differ from the control area in terms of exposure, but the number of samples was low. The power of the study was probably too limited to characterize exposure for this area in comparison with the control area. One positive sample was found in the control area, and it is unlikely that transmission through air from the factory can explain this finding because the control area was located 4.5 km from the soy factory. Trucks would not pass this area. It is more likely that the single positive soy sample of the control area is due to contamination of the sample.

No differences in endotoxin concentrations were found between samples that had been collected downwind from the factory and upwind samples. Sometimes, however, high endotoxin concentrations were encountered in the area surrounding the factory, and these exceeded the provisional threshold level of 90 EU/m³ which has been proposed for the working environment [18]. Especially, the 4 dust samples taken from the factory premises all contained relatively high concentrations of endotoxin.

In Barcelona, a total of 687 persons were affected seriously enough to visit a hospital on days soy beans were unloaded in the harbour [9]. It should be borne in mind that these individuals came from a densely populated area. The resulting potential population at risk for developing health effects must have been large, also because the dust spread over a large surface area in the city. The resulting population at risk likely consisted of several hundred thousand individuals from the downtown Barcelona area. The neighbourhood involved in the city of Utrecht was relatively small. Also, emissions took place at considerably lower height than in the Barcelona area. As a result, exposure to soy bean dust is expected to be low compared to the Barcelonese situation. A direct comparison of soy bean allergen concentrations from Barcelona [10] and from this Utrecht area is however not possible, because allergen detection methods have never been compared. The population at risk in our study was a few ten thousands of individuals at most. The effects shown in this study in a relatively small group of subjects are of a more subtle nature, and will not likely cause hospitalization. Even if they would give rise to hospitalizations, the numbers would be low given the size of the population at risk and these might have been missed as specifically soy exposure related.

Interestingly, parallel to this environmental study, a survey among the workers in the factory was also completed. This survey among 47 out of 70 workers from the factory showed that 5 of the 35 tested by skin prick test for soy sensitization were positive and 31% were atopic. The average exposure of the highest exposed workers involved in unloading was 1 µg/ m³ of soy allergen over a work shift, with a highest value of almost 800 µg/m³. These findings indicate that the workers are considerably higher exposed than individuals living in the vicinity of the factory. These high exposures are accompanied by an elevated sensitization risk.

CONCLUSION

The presented study shows that that exposure to dust from the factory containing soy allergen was associated with a decreased PEF and increased respiratory symptoms in subjects sensitized to soy.

The results of this survey have been reported to the city council. It was later decided by the city to buy out the company and the factory has been relocated to an industrial area. The office buildings have been transformed into a high school.
Acknowledgements
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REFERENCES
2. Ordman D. An outbreak of bronchial asthma in South Africa, affecting more than 200 persons caused by castor bean dust from an oil processing factory. Int Arch Allergy. 1955; 7: 10–24.