Occupational asthma in a steel coating plant

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ABSTRACT An outbreak of occupational asthma, of unknown cause and extent, was detected in a steel coating plant. In 1979 a cross-sectional study which defined occupational asthma in terms of respiratory symptoms detected 21 people with suggestive symptoms among the 221 studied. They all worked in the coating shop, but the plastic coatings used at the plant contained many potential sensitising agents that might have caused the asthma. All 21 developed their symptoms after 1971, and it was found that in this year a supplier had modified a coating allowing, at the temperatures used in the process, toluene di-isocyanate to be liberated. Two of the symptomatic subjects were tested by inhalation of the isocyanate and showed asthmatic reactions and other subjects were found to have asthma related to periods spent at work by records of peak expiratory flow rate. Over half the 21 had a symptom free latent period after first exposure of three years or less, a pattern not seen in other subjects with respiratory symptoms. After the isocyanate had been removed from the process 17 of these subjects became asymptomatic or improved, a greater proportion than in other subjects with respiratory symptoms.

Two men working in a steel coating plant developed symptoms suggestive of occupational asthma. It was necessary to establish if others were affected and to identify the cause in order to recommend appropriate remedial action. An epidemiological investigation was undertaken and the firm was asked to obtain information from its suppliers.

Process

The factory coated rolled steel sheets with coloured plastic by a continuous process on two lines. After rolling, cleaning, and brushing, the steel received a base or prime coat that was cured by passage through an oven, after which a main coat was applied and, again, oven cured. The coated steel, after embossing, was cut up in lengths. The coatings were known to contain epoxy resins, acrylics, phenol formaldehyde, chromates, and polyvinyl chloride. All these and other agents were considered as potential causes of the asthma. The ovens were ventilated during normal operation by an extraction system that discharged into the atmosphere through a

stack. Leakage of vapour could occur around the oven doors and large amounts escaped during breakdowns, when the doors were opened, and during "burn-offs," when an oven was heated to 400°C to remove accumulated condensate from ventilation ducting.

Workforce

The factory employed 241 people, mainly in the coating shop, but also in a separate office building. The largest group employed in the coating shop worked on the two coating lines and had continuous exposure, to, usually, low levels of vapour. The maintenance workers, because they entered ovens after breakdowns, and a group of overhead crane drivers, because they worked above the ovens, were at risk of intermittent, heavy exposure. Other coating shop workers seemed to be less exposed. Some of the office workers visited the coating shop, particularly during breakdowns.

Methods

We initially undertook a cross-sectional study of the entire workforce during one week in October 1979.

The subjects completed a questionnaire and had lung function and skin prick tests performed. So many subjects had work related respiratory symptoms (see below) that they were later asked a second more detailed questionnaire. Random samples of subjects with work related respiratory symptoms, with respiratory symptoms unrelated to work, and without respiratory symptoms were selected and asked to record their peak expiratory flow rate for one month.

QUESTIONNAIRES

The questionnaire answered by all subjects contained sections on respiratory symptoms, smoking, and occupational history. Questions on wheezing, breathlessness, and smoking were taken from the Medical Research Council's questionnaire on respiratory symptoms.¹ A question "Does your chest ever feel tight or your breathing become difficult?" was derived from the questionnaire used to detect byssinosis.² After each of the three questions on respiratory symptoms came questions about the date of onset of the symptom and whether it improved at weekends or on holiday. Symptoms were called "work related" if at least one of the three respiratory symptoms improved at weekends or on holiday. If all the reported symptoms had started either in or after the year the subject joined the factory they were described as starting after employment in the factory. The more detailed questionnaire answered by those subjects with work related symptoms included questions on whether the symptoms had started within a week of either joining the factory or changing jobs in the factory, whether symptoms persisted after leaving work, the duration of attacks of symptoms, the occurrence of attacks during sleep, and the frequency of symptoms. "Occupational asthma" was defined as respiratory symptoms improving at weekends or on holiday, starting after employment in the factory but not within a week of joining or changing jobs, which persisted after leaving work and lasted for at least one hour. Subjects with work related symptoms not meeting these

criteria were described as having "other work related respiratory symptoms" and subjects whose symptoms did not improve at weekends or holidays were described as having "respiratory symptoms unrelated to work." The first questionnaires were distributed by the factory personnel manager and completed by the subjects at home. They were collected by the investigators at the factory and any missing answers filled in at that time or, in some cases, collected by post. An interviewer administered the second questionnaire.

LUNG FUNCTION TESTS

A Vitalograph dry wedge spirometer was used to record forced expiratory manoeuvres from each subject. Readings of forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were taken, using the best of at least two technically satisfactory manoeuvres with FEV₁ and FVC reproducible to within 100 ml. Predicted values based on age, sex, height, and smoking status were calculated from regression equations obtained for use with the Vitalograph.³

SKIN PRICK TESTS

Skin prick tests were performed with cat dander, mixed grass pollen, house dust mite, and *Aspergillus fumigatus* extracts (Bencard). A test was called positive if a weal was observed of at least 2 mm diameter, after subtraction of any weal produced by a control solution, at 15 minutes after testing. A subject was regarded as atopic if at least one such positive test was recorded.

PEAK EXPIRATORY FLOW RATE RECORDS

Fifty subjects were selected by a random selection procedure that aimed to select approximately 50% of those with work related respiratory symptoms, 10% of those with respiratory symptoms unrelated to work, and 5% of those without symptoms. Subsequently, the work related group was divided into those with occupational asthma and those without. Eleven subjects with occupational asthma were cho-

Table 1 Occupational exposure to coating vapours of subjects grouped by symptoms at the first survey

Occupational group	Occupational asthma No (%)	Other work related respiratory symptoms No (%)	Respiratory symptoms unrelated to work No (%)	Asymptomatic No (%)	Total No
Coating line workers	6 (9.0)	25 (37.3)	15 (22.4)	21 (31.3)	67
Overhead crane drivers	2 (20.0)	4 (40.0)	0 (0)	4 (40.0)	10
Maintenance workers	5 (12.5)	11 (27.5)	12 (30.0)	12 (30.0)	40
Other coating shop workers	6 (14.3)	14 (33.3)	8 (19.0)	14 (33.3)	42
Intermittently exposed office workers	2 (5.7)	4 (11.4)	14 (40.0)	15 (42.9)	35
Unexposed office workers	0 (0)	5 (18.5)	9 (33.3)	13 (48.1)	27
Total	21 (9.5)	63 (28.5)	58 (26.2)	79 (35.7)	221

Table 2 Characteristics of subjects by exposure group

Occupational group	Sex M:F	Mean age (years)	Mean employment (years)	Current smokers (%)	Atopic (%)	Mean FEV ₁ (% predicted)	Mean FVC (% predicted)
Coating line workers	1:0	37.5	7.4	64.2	39.4	97.1	98.6
Overhead crane drivers	1:0	41.3	7.6	60.0	40.0	97.1	98.6
Maintenance workers	1:0	30.3	6.0	40.0	37.5	97.9	100.5
Other coating shop workers	1:0	44.4	9.1	59.5	33.3	98.3	100.6
Intermittently exposed office workers	7.8:1	41.5	10.5	37.1	32.4	93.4	95.7
Unexposed office workers	1:2	44.4	12.8	37.0	30.8	97.9	97.9

sen, 28 with other work related symptoms, six with symptoms unrelated to work, and five without symptoms. The subjects were each given a peak expiratory flow rate (PEF) meter (mini-Wright meter or Vitalograph pulmonary monitor) and instructed by one investigator in its use. They noted, on standard forms, the best of three readings every two hours from waking to sleeping every day for four weeks. The four week period included a two week holiday over Christmas and New Year and the working weeks before and after the holiday. From the records, one investigator drew graphs of daily mean, maximum, and minimum PEF as previously described.⁴ Another of the investigators, working without knowledge of the subjects' identities, exposure, or symptoms reported on the graphs, noted whether, in his opinion, the record showed variability of PEF consistent with asthma and whether the record improved during the absence from work. From his reports, records were classified as showing work related asthma, asthma unrelated to work, or no asthma.

STATISTICAL TESTS

The two tailed *t* test for independent samples, the chi squared test with continuity correction, and Fisher's exact test were used for this report. A *p* value of 0.05 or less was taken to be statistically significant.

Cross-sectional survey results

Of the total workforce of 241, 221 (91.7%) returned a questionnaire and 218 (90.5%) had lung

function and skin prick tests. Work related respiratory symptoms were reported by 84 (38.0%) of the 221; this high prevalence occasioned the sending of the second, detailed questionnaire. Using this, 21 (9.5%) had symptoms of occupational asthma and 63 (28.5%) had other work related respiratory symptoms. Fifty eight (26.2%) had respiratory symptoms unrelated to work.

Table 1 shows these symptom groups by occupational group in the factory. None of the unexposed office workers had occupational asthma and the highest prevalence of occupational asthma was in the ten overhead crane drivers, who also had the highest prevalence of other work related respiratory symptoms. Comparing workers exposed to coating vapour with unexposed workers the difference in prevalence of all work related respiratory symptoms was significant (*p* < 0.05).

Tables 2 and 3 show the sex, age, duration of employment, smoking, atopic state, and lung function of the subjects, grouped by exposure and by symptoms. The absence of women in the occupational asthma group is explained by the differing exposures of men and women. All the symptomatic groups had a significantly lower mean FEV₁ than the asymptomatic group but did not differ from each other. Although not significant, the subjects with respiratory symptoms unrelated to work had the highest proportions of current smokers and of atopic subjects. Age and duration of employment did not vary significantly by symptom group.

Figure 1 shows the year of onset of respiratory symptoms in the occupational asthmatics. Nineteen had provided dates of onset of symptoms and these

Table 3 Characteristics of subjects by symptom group

Symptom group	Sex M:F	Mean age (years)	Mean employment (years)	Current smokers (%)	Atopic (%)	Mean FEV ₁ (% predicted)	Mean FVC (% predicted)
Occupational asthma	1:0	41.2	7.7	47.6	30.0	93.0	97.9
Other work related respiratory symptoms	20:1	39.1	7.8	47.6	35.5	95.4	96.6
Respiratory symptoms unrelated to work	5.4:1	39.1	9.3	60.3	43.1	95.6	99.2
Asymptomatic	6.9:1	38.7	8.8	48.1	32.1	100.4	100.5

Fig 1 Date of onset of respiratory symptoms in subjects with occupational asthma.

were between 1972 and 1978. Two had not provided dates but had both joined in 1975.

Comment

At this stage we could say that occupational asthma was confined to those with at least intermittent exposure to coating shop vapours but other work related respiratory symptoms were present in those with and without such exposure. To some extent, both occupational asthma and other work related symptoms were related to degree of exposure to

oven vapours, being most prevalent, although this was a small group of only 10 men, in the crane drivers who worked over the ovens. These observations gave no clue to which of the many substances in the oven vapours was causing these symptoms, and the personal characteristics of the occupational asthmatics were unremarkable. The dates of onset of their symptoms, however, all after 1971, suggested that a change had occurred in the process at about this time that might have caused the asthma.

Focusing their inquiries on possible changes at this time, the factory management discovered that one of their suppliers had modified a prime coat in 1971 so that from this date toluene di-isocyanate (TDI) was liberated during the curing process. It seemed that this well known and potent sensitising agent might have caused the asthma at the plant, and it was decided to admit the two index cases to hospital for inhalation challenge testing.

Meanwhile, the workforce at the factory had joined in a national strike in the industry of which this factory was a part. The start of the strike coincided with the recording period for the PEF records and it did not end for many weeks afterwards. This interfered considerably with the motivation of the subjects to continue records and with the collection of the records, which was done by post after telephoning or writing to those subjects whose addresses were available. It was judged important to collect as many records as possible, as this was the only way of confirming work related asthma in those subjects who did not have an inhalation challenge test.

In October 1979 environmental levels of TDI

Table 4 PEF record assessment by symptom group

Symptom group	PEF assessment			
	Work related asthma	Asthma unrelated to work	Normal	Total
Occupational asthma	3	1	1*	5
Other work related respiratory symptoms	1	9	2	12
Respiratory symptoms unrelated to work	1	3	0	4
Asymptomatic	0	2	1	3

*Subject of fig 2 without exposure to TDI during the recording period.

Table 5 Timing of the date of onset of occupational asthma

Latent period (years)	Occupational asthma	Other work related respiratory symptoms	Respiratory symptoms unrelated to work
8	0	1	1
7	3	4	3
6	0	2	2
5	2	2	1
4	3	4	2
3	3	2	1
2	2	1	1
1	4	3	2
<1	2	3	0
Before 1971	0	1	2
Total	19	23	15

Fig 2 Results of inhalation testing with TDI and control in one of the patients tested.

were measured using static bubbler samplers containing ethanol with subsequent analysis by high pressure liquid chromatography. Concentrations during normal processing were measured and also levels during line stoppages of five, 30, and 60 minutes. In April and May 1980 burn offs were carried out to remove residual TDI from the ovens and sampling was repeated.

When the plant returned to normal, working conditions were identical except for the absence of TDI. A second cross-sectional survey was performed after the return to work in July 1980. Only those with some exposure to coating shop fumes were asked to participate on this occasion. All subjects had a questionnaire to answer and again those with work related symptoms also answered a more detailed questionnaire, which included questions on the date of the last attack of symptoms and on the subject's opinion on whether his symptoms had improved, deteriorated, or remained the same since the first survey. Subjects were regarded as asymptomatic if they no longer reported symptoms or if they reported the last attack as occurring at least five months before the second survey. To assess change between the surveys, the questions on frequency of attacks during sleep, of attacks in general, and the subjects' own assessments of change, were used. The highest frequency of any respiratory symptom was used. If at least one measure had improved, symptoms were regarded as improved and similarly for deterioration. If one measure had improved, one deteriorated, and one remained the same the symptoms were regarded as unchanged.

Further results

INHALATION CHALLENGE TESTING

Inhalation challenge testing was performed with

TDI and a control using a standard two part varnish test.⁵ Neither subject showed any reaction to the control test and both showed falls in FEV₁ of at least 15% of the baseline several hours after testing with TDI. One of these tests is illustrated in fig 2. Both of these subjects had been classified as having occupational asthma by the questionnaire.

PEF RECORDS

Only 24 (48%) of the 50 subjects returned records. Five were classified as showing work related asthma, 15 as asthma unrelated to work, and four as normal. The results of PEF measurements from one subject thought to show work related asthma are illustrated in fig 3. Symptom group and PEF record

Fig 3 Graph of daily mean, maximum, and minimum PEF in one subject with occupational asthma. Arbitrary units used for PEF approximate to litres/minute, but at this time the Vitalograph pulmonary monitor, used by this subject, had not been finally calibrated. Subject was on strike for most of this record.

Table 6 *Environmental concentrations of TDI around the prime oven*

Sample timing	Sampling site		
	Oven entry	Oven exit	Above oven
Normal processing	0.014*	0.001	0.010
5 minute stoppage	0.026	0.007	0.014
30 minute stoppage	0.002	0.002	<0.001
60 minute stoppage	0.015	<0.001	0.006
Normal processing (after burn offs)	<0.001	0.002	<0.001

*All concentrations in ppm. The 1979 eight hour TWA was 0.020 ppm. The 1984 eight hour TWA for difunctional monomeric isocyanate is 0.005 ppm and 10 minute TWA 0.020 ppm.

classification are compared in table 4. The subject whose asthmatic reaction after inhalation of TDI is shown in fig 2 had no coating shop exposure during the recording period and had a normal PEF record. Excluding him, the association between occupational asthma and work related asthma in the PEF record is statistically significant and remained so if those who had not returned records were assumed to be normal and included in the analysis.

LATENT PERIODS OF RESPIRATORY SYMPTOMS

The symptoms of the occupational asthmatics had, by definition, started after they had joined the factory. They were compared with those with other work related symptoms and those with symptoms unrelated to work whose symptoms had also started after joining. Dates were provided by 19 of 21 occupational asthmatics, 23 of 30 people with other work related symptoms, and 15 of 33 subjects with symptoms unrelated to work. A latent period of symptom free exposure was obtained by subtracting from the year of onset of symptom, the year of joining the firm, or the year of introduction of TDI, 1971, whichever was the later. Table 5 shows that symptoms in over half of the occupational asthmatics started within three years of exposure to TDI, but the distribution of latent period in the other symptom groups did not show this pattern and in some subjects symptoms had preceded exposure to TDI.

ENVIRONMENTAL TDI LEVELS

Table 6 shows the TDI concentrations at three sites around the prime oven during normal processing, during stoppages of different duration, and after burning off residual TDI. Concentrations rose considerably during a five minute stoppage and declined with stoppages of longer duration. No short term exposure limit was currently recommended but levels approached or exceeded the current eight hour TWA of 0.020 ppm that has since become a 10 minute TWA. Under working conditions, concentrations could have been higher if oven doors were opened during a line stoppage.

FOLLOW UP SURVEY

Of the 221 original subjects, 184 (83.3%) were seen again. Of those not seen, 25 unexposed office workers were deliberately excluded, so the true response rate was 93.9%. No new occupational asthma had developed among those seen for the second time. In addition, ten of the original 20 non-responders and one new employee were seen and none of these had occupational asthma.

The change between the two surveys could be assessed in the occupational asthmatics and in those with other work related symptoms. Table 7 shows that similar proportions (40.0% and 39.3%) were now asymptomatic but of those with continuing symptoms, more occupational asthmatics (45.0%)

Table 7 *Changes in symptoms after TDI removal*

Symptoms in 1980	Symptoms in 1979	
	Occupational asthma No (%)	Other work related respiratory symptoms No (%)
No symptoms	8 (40.0)	22 (39.3)
Symptoms unrelated to work:		
Better	2 (10.0)	0 (0)
Same	1 (5.0)	3 (5.4)
Worse	0 (0)	1 (1.8)
Total	3 (15.0)	4 (7.1)
Symptoms related to work:		
Better	7 (35.0)	10 (17.9)
Same	2 (10.0)	15 (26.8)
Worse	0 (0)	5 (8.9)
Total	9 (45.0)	30 (53.6)
Total	20	56

Table 8 Occurrence of symptoms during sleep at the two surveys

Symptom frequency	Occupational asthma		Other work related respiratory symptoms	
	1979	1980	1979	1980
Most nights	4	0	0	1
Weekly	1	0	0	0
Occasionally	6	3	18	8
Never	9	14	27	41
Total	20	17	45	50

reported improvement than did those with other work related respiratory symptoms (17.9%), and no occupational asthmatics compared with 10.7% of those with other work related symptoms reported deterioration. The tendency to cessation or improvement of occupational asthma was statistically significant. The continuing symptoms remained work related in 45.0% of those with occupational asthma and in 53.6% of those with other work related symptoms.

The most striking change in individual symptoms was seen in the question about symptoms waking subjects from their sleep (table 8). In 1979, 25% of the occupational asthmatics were waking at least once a week with symptoms but none of those with other work related symptoms. In 1980 none of the occupational asthmatics was waking more than occasionally, but one with other work related symptoms was waking most nights.

Discussion

The study is interesting as an example of the use of epidemiological methods in the investigation of an outbreak of asthma and both the study design and the measurements taken need examination. A cross-sectional design was chosen for the sake of speed and simplicity, but this type of study is likely to underestimate the scale of such outbreaks. Workers with occupational asthma tend to leave the job that causes their symptoms and probably in the eight years since TDI had been introduced some, perhaps many, affected individuals had already left the plant. It was not feasible to trace past employees in order to perform a longitudinal study but this might have been a more appropriate design to estimate the true size of the outbreak. The 21 occupational asthmatics must be regarded as the minimum number of people affected.

In clinical practice in the United Kingdom the patient's history is used to make the diagnosis of occupational asthma and it may be supplemented by lung function measurements to confirm work related physiological changes and by demonstration of reactions against specific occupational antigens. The types of measurement used in this study closely fol-

lowed clinical practice, with occupational asthma being defined in terms of symptoms, work related asthma confirmed by PEF records, and bronchial reactions against TDI shown in inhalation tests.

Any definition based on symptoms is necessarily subjective. It might be argued that subjects with heavy exposure to coating vapour would be likely to overreport symptoms and to magnify their severity, which might have produced the increased prevalence of occupational asthma symptoms in those working in the coating shop. But as no-one, including the subjects, knew at this stage that TDI had been introduced in 1971, subject bias cannot explain the onset of occupational asthma after 1971 nor can it explain the tendency for a short latent period of three years or less seen in the occupational asthmatics. By the second survey it was generally known among the workforce that TDI had been present and had now been removed. A clinical categorisation of the workforce, using all available information, was not prepared until after the second survey, but many of the subjects with occupational asthma must have realised before then that they had asthma caused by TDI. Therefore, it might be argued that the greater improvement among them was explained by their expectation of improvement with removal of TDI. We do not think that this was the case because our impression was that these subjects remained more concerned about their health than others, even after TDI was removed, and if anything, were more likely to exaggerate than diminish their symptoms.

In addition to their subjectivity, respiratory symptom questionnaires may also be non-specific, and many subjects in this population had work related respiratory symptoms that were not caused by occupational asthma. Some probably had chronic bronchitis or asthma without occupational cause and found that coating vapour irritated their respiratory tracts which led to exacerbations of their symptoms at work. Others without respiratory disease probably were transiently irritated by high concentrations of coating vapour. This non-specific production of work related respiratory symptoms by industrial environments leads to diagnostic problems in clinical practice, and in surveys leads to dilution of

subjects with occupational asthma by subjects without. We therefore used our second more detailed questionnaire, and possibly we increased specificity at the expense of sensitivity and failed to detect some subjects who truly had occupational asthma. For example, we rejected subjects who reported respiratory symptoms before they joined the coating plant. Although most of these probably did not have occupational asthma, some may have, and had unrelated respiratory symptoms before they joined the firm.

Our definition received confirmation from PEF records. It might be thought that PEF records should be used as the primary investigative measure in outbreaks of occupational asthma, and such an approach has many attractions, but this study illustrates two problems with this approach. Firstly, physiological changes of work related asthma can be detected only if the relevant exposure occurs during the record. The subject whose inhalation test with TDI is illustrated in fig 2 had a normal PEF record as he did not work in the coating shop during this period. Many occupational asthmatic subjects are relocated or relocate themselves at work to lessen their exposure to the cause of their asthma. Secondly, compliance with PEF records will be less than with simpler investigations such as questionnaires. Compliance was poor in this study because of the strike and an effect of poor compliance was well illustrated, an apparent overestimation of the prevalence of asthma. Subjects with asthma find that their PEF readings vary considerably, and this increases their interest in the record and their compliance. Subjects without asthma find that their readings are similar and tend to lose interest and fail to complete the record.

Confirmation of the definition and also of TDI as the cause of occupational asthma was seen in the results of inhalation testing with TDI. Inhalation testing is not suitable as a mass screening test for working populations, but skin tests and serological tests for antibodies are easily used for this purpose. Such tests are not available for the isocyanates,

although promising preliminary immunological studies are in progress, but they are available for other occupational antigens. The demonstration of reactions to antigen in skin or in blood is a much less direct confirmation of occupational asthma than the demonstration of a bronchial reaction in inhalation tests, and both false positive and false negative tests are likely.

We think that, despite its potential problems, this study played a valuable part in investigating this outbreak. It placed the cause in the coating shop and timed the start of the outbreak as 1972. This led to the discovery that TDI had been introduced in 1971. Both the cause of the asthma and the definition used in the survey were validated in the course of the study. The removal of TDI led to improvement of symptoms, further confirming TDI as the cause, and continued follow up of the workforce has shown that this outbreak is now over.

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