Climate, intermittent humidification, and humidifier fever

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ABSTRACT Two summer outbreaks of humidifier fever (HF) are described in a microprocessor factory (factory A) and a printing factory (factory B). The air in each factory was humidified intermittently and controlled by preset humidistats operating to maintain a relative humidity of 45% by an air handler incorporating a spray humidifier in factory A and two ceiling mounted spray humidifiers in factory B. Questionnaire data from each workforce suggested that although symptoms apparently occurred most commonly in both factories on return from holiday (41/57, 71.9%), many subjects (24/40, 60%) in factory A also had intermittent symptoms of ill defined periodicity for some time before the disorder was recognised. Similar intermittent symptoms with no discernible pattern occurred in factory B in a smaller number of subjects (4/17, 23.5%), all of whom were night or rotating shift workers. Both episodes of humidifier fever after return from summer holiday developed when nocturnal air temperatures were unseasonably low; not on the day of return to work but two days later (factory A) and one day later (factory B). Symptoms were most common in those workers who had circulating serum IgG antibody measured by ELISA to humidifier sludge in factory B (14/17, 82.9%) but were most common in IgG antibody negative subjects in factory A (27/40, 67.5%). A more classic form of humidifier fever redeveloped in factory B during winter when meteorological recordings suggested that humidification of intake air was more continuous. Humidifier fever in winter may have been the major influence on the formulation of the symptom pattern thought to be relevant for recognition of the disorder. A form of the illness, however, can occur during the summer which is camouflaged by intermittent humidification when the symptoms appear to be more closely associated with cool nocturnal air intake and unrelated to the pattern of attendance at work.

Humidifier fever is said to occur in susceptible individuals on the first day of return to work after a break and is characterised by influenza like symptoms of pyrexia, lassitude, cough, chest tightness, and dyspnoea which appear after exposure to the output from a contaminated humidification system.¹ These symptoms usually become less troublesome as the working week progresses. The disease has been primarily recognised as a winter illness,² supposedly because of the greater use of humidifiers when the air intake to a ventilation system is coolest. Two factory outbreaks of humidifier fever which occurred during summer and which correlated precisely with low external air temperature measurements are discussed.

Patients and methods

Two factories were investigated where workers had

been affected by illness which appeared to be work related. The medical officer in one factory suggested a recurrence of humidifier fever because of experience of a similar outbreak three years previously.³ Both factories were visited by two of the authors (KA and ADW) on the day after problems with the health of the workers in each factory were noted and were visited again on several occasions during the following week when a doctor administered questionnaire was completed with symptomatic workers in factory A and all workers exposed to artificially humidified air in factory B. Symptoms were noted for the period after the holiday or over the previous four months. The questionnaire detailed systemic and respiratory symptoms and the timing of these symptoms, age, duration of employment, and smoking history.

These subjects then gave a venous blood sample. The serum was analysed by enzyme linked immunosorbent assay (ELISA) against humidifier water from

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Table 1 Symptoms recorded in each factory showing the total number of subjects with each symptom and the presence of specific IgG antibody (ELISA +ve) found in conjunction with the symptoms

	Factory A		Factory B	
	No of subjects	ELISA + ve	No of subjects	ELISA + ve
Chest tightness	15	7	13	10
Headache	24	9	4	3
Chills	17	7	13	9
Breathlessness	15	5	3	3
Cough	18	4	1	1
Wheeze	11	4	0	0
Poor appetite	10	5	0	0
Weight loss	6	4	0	0
Fever	8	7	13	9
Tiredness	26	11	0	0
Total No of symptomatic subjects	40	13	17	13

each factory. The sera were incubated overnight at room temperature in microtitre plates coated with humidifier water. Alkaline phosphatase conjugated monoclonal anti-human IgG was then added. After further incubation sigma 104 phosphatase substrate was added and after colour development the optical density (OD) values were read at 405 nm using a Titertek Multiscan ELISA reader. The results were expressed semiquantitatively using a specific binding index (SBI).

$$SBI = \frac{OD_x - OD_{LC}}{OD_{HC} - OD_{LC}} \times 100$$

where OD_{HC} = OD of positive control

OD_{LC} = mean OD of negative controls + 2SD

OD_x = OD of unknown sample

Table 2 Periodicity of symptoms in each factory according to questionnaire data showing the number of subjects and the total of subgroup who had specific IgG antibody (ELISA +ve). Holiday return symptoms do not preclude intermittent symptoms in the same subject, therefore the column titled "No of subjects" exceeds the number of symptomatic subjects in each factory

	Factory A		Factory B	
	No of subjects	ELISA + ve	No of subjects	ELISA + ve
Symptoms on return from holidays	26	8	15	12
Intermittent symptoms through working week	24	13	4*	4
Unsure	4	2	1	1

*Three night shift, one rotating.

Table 3 Serology in each factory according to shift worked

Shift	Factory A		Factory B	
	ELISA + ve	ELISA - ve	ELISA + ve	ELISA - ve
Day	11	18	10	8
Night	2	3	3	0
Rotating	0	6	1	0

Further details of the ELISA technique will be published elsewhere (Lewis C, *et al*). In the present paper the serology is presented as either ELISA positive or negative.

Results

FACTORY A

Factory A was a microprocessor factory (employing more than 1000 people) with a sealed ventilation system incorporating various air purification filters supplying conditioned air to partitioned testing and assembly areas. The air handling unit (American Air Filters) which supplied the area under examination had been installed in 1976 and contained a water storage bath which supplied water jets. This unit was modified in 1983 after previous humidifier fever by attaching a drainage outlet to the bath to reduce water recirculation. The water spray was controlled by a humidistat to maintain a humidity of at least 45% to prevent static electricity. The precise water consumption of the unit was not known, however. The maximum air flow capacity was 14.4 m³/s with an estimated average airflow in winter of 5 m³/s and water consumption of 95 l/day varying according to the degree of air recirculation and the temperature of the external air intake. Summer water consumption was not known but was thought to be a small fraction of the winter figure. Forty workers who complained of symptoms (out of 250 who were known to work within the area served by the contaminated unit) were identified with the help of the factory medical service. These symptoms (table 1) were most prominent two days after returning to work from the summer holiday in July 1986. Many workers, however, described similar symptoms which had occurred irregularly over the previous four months, which were of intermittent nature, of no specific pattern, and less clearly work related (table 2). Circulating specific IgG antibody was detected by ELISA (table 3) to humidifier water in 13 subjects (32.5%) but more subjects had no measurable circulating specific IgG (27/40, 67.5%). Within the group there were no relations between age, duration of employment, or sex and the development of symptoms or positive serology. Only 6/40 were cigarette smokers of whom one was ELISA positive. In that case we confirmed inhalation of cigarette smoke by finding a carboxyhaemoglobin of 8%.

Minimum and maximum temperatures for relevant periods for outbreaks of humidifier fever in factory A (1986) and factory B (1985 and 1987) indicating day of return from holiday (small arrow) and day of onset of symptoms (large arrow). Estimated temperature below which humidifiers operated is marked at 10°C. Temperature recordings were adapted with permission from HM Metereological Office records.

FACTORY B

Factory B was a printing factory of barn design with natural ventilation employing 30 people. The fresh air intake was heated to 17°C and a relative humidity of 45% (to avoid paper shrinkage and creasing) was maintained by two ceiling mounted spinning disc humidifiers (WEKO, type LDFT, Biel AG), controlled by a wall mounted humidistat. The maximum water consumption of each humidifier was 7 l/h but the actual water consumption was unknown. Both humidifiers were found to be heavily contaminated by vegetable starch ("anti-offset powder") and to contain viscid fluid. All 22 individuals who were exposed to the contaminated humidifiers were assessed, of whom 17 were symptomatic. The others worked in a naturally ventilated office distant from the humidified area and were not assessed. The 17 subjects complained of symptoms which were noted one day after returning from the annual summer holiday in July 1985 (table 1). Symptoms had occurred previously for a longer period in four subjects who commented that these symptoms seemed more common when working on the night shift (table 2). Circulating specific IgG antibody to humidifier water was detected in 13 symptomatic subjects (ELISA positive) and absent in four others (ELISA negative) who also had symptoms (table 3). Two asymptomatic subjects were ELISA positive. There were no significant differences within the symp-

tomatic and asymptomatic groups or for subjects who had circulating specific IgG (ELISA positive) and those without for age, duration of employment, or sex. Of the 7/22 who smoked cigarettes, five had circulating specific IgG. Only one of the smokers and three non-smokers were both asymptomatic and also ELISA negative. A further outbreak occurred on the day of return to work from the winter holiday in January 1987 when the symptoms were recognised on the day of return to work as a recurrence of the humidifier fever when similar medical assessment was performed (results not shown).

CLIMATOLOGICAL CONSIDERATIONS

The meteorological office serving the Glasgow area is at Glasgow Airport (Abbotsinch). Measurements of air temperature and humidity are taken hourly and the records retained for future reference. The daily minimum and maximum dry bulb temperatures for the relevant periods (factory A, July 1986; factory B, July 1985 and January 1987) are shown in the figure (J Allardyce, Glasgow Weather Centre, personal communication).

Discussion

Humidifier fever is likely to be more common in the winter months² when air conditioning plants operate in a more continuous fashion.⁴ The external air temperature in summer, however, is occasionally low enough to require the addition of water after the air intake is heated. In general terms, when the air temperature is increased by 10°C the relative humidity is reduced by half.⁴ The humidifiers in factories A and B would then operate when the external air temperature is less than about 10°C to maintain humidity at 45% (the activation temperature was estimated at 8–12°C depending on moisture content of the air intake). These temperature variations cannot follow the working week and hence the expected pattern of humidifier fever, with symptoms at the beginning of a working week which recede thereafter, would not occur. Our groups of workers did complain of symptoms after returning from holiday but this statement is imprecise. Symptoms developed on the day after (factory B) and two days after (factory A) the annual holiday, only when (we assume) the humidifiers were switched on by the low nocturnal temperatures. Further examination of temperature records shows that such nocturnal temperatures are unusual but not uncommon in spring and summer⁵ and probably explain the intermittent nature of the symptoms in some subjects.

Our night shift workers complained of symptoms more often than the day shift which we presume was

caused by intermittent humidification in response to the lowest daily temperatures. A previous outbreak of humidifier fever in factory A was investigated in 1983 with another assessment nine months after the initial problems were corrected.³ Most of the affected workforce recovered quickly but a small group of workers had persistent symptoms which were not adequately explained, and all were night shift workers. Some time later it arose that the contaminated air handler had been used on an emergency basis when maximum humidification was required.

In factory A subjects may have also described symptoms in keeping with extrinsic allergic alveolitis or asthma which have been reported in association with contaminated ventilation systems.^{6,7} These symptoms, however, were not recognised as work related until humidifier fever developed.

The aetiology of symptoms in the antibody negative group could be related to intermittently large antigen release from a previously dormant humidifier. Finnegan and Pickering have suggested that non-sensitised individuals occasionally develop symptoms, possibly in response to a high antigen load,¹ a response that may be similar to a disorder which has been described in farmers.⁸ We speculate that this type of reaction in non-sensitised workers is a feature of intermittent humidification.

Almost 30 years have elapsed since humidifier fever was first associated with a contaminated ventilation system⁹ and the precise aetiology remains uncertain.¹⁰ Recently, other forms of humidifier illness have been described^{6,7,11,12} in the United Kingdom, some of which had been reported previously in North America.¹³ The present paper describes a summer form of humidifier fever that occurs as a result of intermittent humidification with symptoms that might not appear work related because of an irregular, non-working week

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symptom pattern. We would recommend that humidifiers should be serviced at least as often during the period of lesser activity in summer (or perhaps more often) as in winter to avoid organic contamination.

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