Scand J Work Environ Health 1979;5(1):35-41

<https://doi.org/10.5271/sjweh.2673>

Issue date: Mar 1979

Humidifier-associated extrinsic allergic alveolitis.

by [van Assendelft A](#), [Forsén K-O](#), [Keskinen H](#), [Alanko K](#)

Key terms: [Amoeba proteus](#); [Aspergillus fumigatus](#); [Thermoactinomyces vulgaris](#); allergic alveolitis; cool-mist humidifier; extrinsic allergic alveolitis; humidifier

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/375386

This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

Humidifier-associated extrinsic allergic alveolitis

by A. VAN ASSENDELFT,¹ K.-O. FORSÉN,² HELENA KESKINEN,³
and KARI ALANKO³

ASSENDELFT, A. VAN, FORSÉN, K.-O., KESKINEN, H. and ALANKO, K. Humidifier-associated extrinsic allergic alveolitis. *Scand. j. work environ. & health* 5 (1979) 35-41. Three cases of allergic alveolitis due to indoor humidification systems are described. *Thermoactinomyces vulgaris* precipitins were detected in the serum of a 37-year-old female patient who had typical febrile attacks during exposure to cool-mist from a home humidifier. When the cause was detected and eliminated, the symptoms and signs disappeared and the woman's gas transfer factor improved from 56 % to normal within six months. In a printing office a 60-year-old woman had had febrile attacks with cough for more than a year. The patient herself associated the respiratory disease with a cool-mist humidifier sometimes used at work. The water reservoir was heavily contaminated with amoebas (*Amoeba proteus*), which might have been the causative organisms in this case. *Aspergillus fumigatus* precipitins were found in the serum of a 53-year-old female printer with the clinical picture of occupational allergic alveolitis. The same organism was detected in the ambient air of the printing office.

Key words: allergic alveolitis, cool-mist humidifiers, humidifiers, *Thermoactinomyces vulgaris*, *Aspergillus fumigatus*, *Amoeba proteus*.

Immunologic responses to inhaled organic dust vary. Usually an immediate asthmatic reaction (type I) develops, but occasionally immunocomplex-related allergic alveolitis (type III) is seen. Farmer's lung, a granulomatous pneumonitis for which precipitating antibodies can be shown against thermophilic actinomycetes in the serum of the patient, is a typical example of the latter (15).

Many causative organisms can be found in dusts containing molds, spores and bacteria. Sensitization to these organisms usually occurs when a person works under dusty conditions, but it is also possible for allergic alveolitis, e.g., bird fancier's lung, to develop at home (18). Recently hypersensitivity pneumonitis related to air-conditioning or humidification systems has been reported in several studies (table 1). The cases presented in our report reveal a similar phenomenon.

In such cases profound knowledge of both the clinical features involved and the existence of adequate exposure are essential for diagnosis. Also immunologic and physiological examinations are helpful. Finally, if other measures have been ineffective, a provocation of the clinical symptoms by controlled exposure challenge can be considered.

¹ Department of Pulmonary Diseases, North Karelian Central Hospital, Kontioniemä, Finland.

² Mjölbolsta Hospital, Mjölbolsta, Finland.

³ Department of Occupational Medicine, Institute of Occupational Health, Helsinki, Finland.

Reprint requests to: Dr. Kari Alanko, Lahti Central Hospital, SF-15900 Lahti 90, Finland.

Table 1. Previously reported cases of extrinsic allergic alveolitis caused by contaminated air-conditioning systems and humidifiers.

Author	Number of cases	Probable causal agent	Time from beginning of exposure to development of illness	Precipitins
Pestalozzi (16)	14	Mold fungi <i>Micropolyspora</i>	?	Not taken
Banaszak et al. (2)	4	<i>Micropolyspora faeni</i>	?	Against an extract of the specific thermophilic organism cultured from the air-conditioning system + moldy hay
Weiss and Soleymani (23)	1	Thermophilic actinomycetes	About 3 months	Against one of the thermophilic fungi
Fink et al. (4)	1	<i>Micropolyspora faeni</i>	?	Against a saline extract of the thermophilic actinomycetes cultured from the water of the humidifier
Sweet et al. (21)	1	Thermophilic actinomycetes	Less than 6 months	Against a 10% w/v saline extract of the organism isolated from the furnace humidifier
Tourville et al. (22)	1	<i>Thermoactinomyces vulgaris</i>	?	Against an extract of the involved <i>Thermoactinomyces vulgaris</i> isolated from the humidifier
Keller et al. (10)	5	Thermophilic actinomycetes	?	In one case against an extract of the water from the humidifier of another patient
Hodges et al. (7)	1	?	?	Against the water of the humidifier
Marinkovich and Hill (13)	1	<i>Micropolyspora faeni</i>	?	Against <i>Micropolyspora faeni</i> and mold extract
Pickering et al. (17)	9	Mold fungi	5 months to 3 years	In eight cases against the baffle plate "jelly" and in six cases against <i>Thermoactinomyces viride</i>
Miller et al. (14)	1	?	4 weeks	Against the central humidifier water
Burke et al. (3)	2	<i>Thermoactinomyces vulgaris</i> <i>Thermoactinomyces candidus</i>	1—2 years	Against both thermophilic actinomycetes cultured from the water of the humidifier in one case and against the undiluted humidifier water in the other

CASE HISTORIES

Case 1

A 37-year-old nonatopic gymnastic teacher with no previous diseases became ill on 22

January 1976 after returning from a holiday in the Canarian Islands. The symptoms were chills, headache, and malaise. Her temperature rose to 40°C in the night and returned to normal during the day. The symptoms repeated themselves during

the next few nights and were connected with an irritating cough with some yellowish sputum and dyspnea. Because the symptoms continued despite tetracycline and amoxicillin therapy, she was admitted to the Mjölbolsta Hospital on 2 February 1976.

A physical examination on admission showed a tired patient who, in two weeks, had lost 4 kg. She had a dry irritating cough, her expiration was wheezy, and crepitant rales were present at both lung bases. Her temperature was 37.5°C. The fever and the other symptoms disappeared after a couple of days in the hospital. The fever during the hospital stay and before admission can be seen in fig. 1.

A chest radiograph showed bilateral, diffuse nodular interstitial infiltration. The erythrocyte sedimentation rate (ESR) was 26 mm/h, the hemoglobin concentration 138 g/l, and leucocytes $18.4 \cdot 10^3/\text{mm}^3$ with 80% neutrophils. No eosinophilia was present. Sputum cultures revealed no pathogenic bacteria. Blood cultures were negative. Virus antibodies were not detected. Hypergammaglobulinemia was not present. The total amount of the immunoglobulin IgE was normal, and no IgE antibodies were found that were specific to house dust. The Waaler-Rose and latex fixation tests were normal.

Pulmonary function tests showed changes which suit an interstitial lung disease; i.e., a slightly subnormal vital capacity (3.29 l or 82% of the predicted value); slight arterial hypoxemia, which became worse with exertion (pO_2 from 67

to 59 mm Hg); and a clearly diminished transfer factor (13.2 ml CO/min per mm Hg, which is 56% of the predicted value).

Since the patient developed the symptoms during the weekends when she was permitted to leave the hospital (fig. 1.), we began to suspect extrinsic allergic alveolitis caused by a domestic factor. A careful inquiry revealed that in October of 1975 the patient had begun to use a poorly cleaned cool-mist atomizer type of humidifier in her bedroom. Before this time the humidifier had been stored in a shed for two years. During the autumn the patient had felt inexplicably tired. This fatigue continued, in spite of her holiday after the New Year, and culminated in the aforementioned symptoms. In the water of the humidifier, and in a film which covered the inside of it, there were large amounts of many different types of fungi, some acinebacter, and a few bacteria of the bacillus family.

After the humidifier was cleaned with disinfectant, no symptoms were detected. But after some days, during which the humidifier was not used, the symptoms reappeared. With the same humidifier the clinical symptoms were provoked in the hospital 8 h after the beginning of the exposure challenge.

Precipitins against *Thermoactinomyces vulgaris* were found in the patient's serum, but none appeared against *Aspergillus fumigatus* or *Micropolyspora faeni*. A cutaneous test with *Aspergillus fumigatus* was also negative.

Fig. 1. Case 1: Fever curve and changes in the erythrocyte sedimentation rate (ESR) recorded for a 37-year-old patient during her stay at a hospital and intervening intervals at home. The period marked with an x was immediately preceded by an attempt to clean the humidifier.

The patient's history and the results of the investigations are consistent with a diagnosis of extrinsic allergic alveolitis caused by thermophilic actinomycetes which had spread into the air from the contaminated humidifier. The patient replaced the humidifier with one of the steaming type, and she has remained without symptoms ever since. Her ESR decreased to 4 mm/h, and her blood values and partial oxygen pressure (pO_2) became normal. In two months her carbon monoxide diffusing capacity rose from 56 to 78 % of the predicted value, and after six months it was normal.

Case 2

A 60-year-old female bookbinder with no history of allergy had been in the same profession for 30 years and had been employed by the same enterprise for 11 years. During the last 1.5 years she had intermittently had a fever of up to 39°C. It rose fast, usually in the evening after she returned home from work, and disappeared by morning. Cough was the only symptom connected with the fever. The patient associated the symptoms with a humidifier which was sometimes used at her place of work. The symptoms came only after days when the humidifier was on. It was a cool-mist atomizer type of humidifier. Its rotating blade and other upper parts were covered with a dry film. In addition the water in the reservoir was slimy, and a microscopic investigation revealed a lot of vigorously moving amoebas 1–5 μ in diameter. They were identified as probable *Amoeba proteus* at the Parasitology Laboratory of the Aurora Hospital, Helsinki.

The patient had leucocytosis, her ESR had risen to 43 mm/h, and her chest radiograph showed slight interstitial infiltration in both lungs. Spirometry was normal. Amoeba antibodies were negative. Farmer's lung antibodies were not taken. The patient's symptoms vanished after the practice of cleaning the humidifier with a 4 % formalin solution was initiated.

Case 3

Case 3 was a 53-year-old female printer who had a 3- to 4-year history of allergic

rhinitis during the springtime, for which she had received specific hyposensibilization treatment with good effect. She had had a bird at home for the past 10 years. She had worked as a printer for the same employer since 1973. Two years ago she began to run a fever, about 39°C, in the afternoon of some workdays. During the last year dyspnea was also connected with the fever as was also muscle pain and poor appetite. On her first workday after her summer vacation in 1978, during which she had been without symptoms at home, she ran a high fever and experienced severe dyspnea in the afternoon. Crepitant rales were heard, and she was sent for investigation.

The patient came to the hospital straight from her job. Except for the crepitant rales, her physical status was normal. Her spirometric values were also normal, but her transfer factor was 67 % of the predicted value. After a week in the hospital the rales were no longer present and her transfer factor was within normal limits. Histamine did not cause bronchial hyper-reactivity. Skin tests with common allergens administered with the prick method showed several positive pollen reactions, which were already known. The intracutaneous tests with molds gave several positive immediate reactions, e.g., in the case of *Aspergillus fumigatus*, *Cladosporium*, *Fusarium*, *Penicillium*; but no delayed reactions with molds were seen.

The work environment of the patient was investigated. To keep the ambient air at the optimal humidity, an atomizing humidifier was located about 2 m from the patient. Mold cultures were taken from the air of the office, and a rich growth of *Aspergillus fumigatus* was seen. Other molds (*Mucor*, *Penicillium*, *Cladosporium*) and bacterial growth (*Streptococcus non-hemolyticus*, *Faecalis alcaligenes* and *Chinobacter*) were found in the slime of the atomizer. No amoebas were found.

Once the patient had recovered, a workplace provocation test was made in which her physical status, temperature, peak expiratory flow values, and leucocyte and eosinophil cell counts were followed for 2 d. During the first test day the patient's temperature began to rise after 6 h and was highest after 8 h. No rales were heard. Her temperature was normal the next

morning. During the second day she did not have a fever, but crepitant rales were heard. There were no changes in her transfer factor. The radiological examination continuously revealed normal results.

Precipitant antigens to *Aspergillus fumigatus* were found in the serum of the patient; the avian precipitins were positive also. The patient's history indicated that an occupational etiology for the allergic alveolitis was more probable than bird fancier's disease. In any case, she was requested to give her bird away.

After the humidifier in the printing office was cleaned, the patient returned to work, but again she got a fever on the first afternoon. She was given another job. It will probably take time to get the molds cleaned from the office.

HUMIDIFIERS

In Finland 14 manufacturers had a humidifier on the market in 1976. In addition there are different types for office and factory use, the biggest of which are completely automatic air-conditioning systems that heat, cool, clean, humidify and dry according to need.

The humidifiers now in use work according to one of three principles: (a) evaporation, (b) cool-mist atomizing, and (c) steaming. In evaporation humidifiers the water is lifted on a filter or carpet, from which it is spread into the air by a screw. In this way the water is cleaned of dust, lime, etc. However, the filter gets dirty and must be changed regularly. Evaporators have been connected to heat elements in an effort to make them more effective. With cool-mist atomizers the water is separated into drops by a dispersing cylinder or is mixed into the air with a centrifugal machine.

All the humidifiers to which extrinsic allergic alveolitis has been associated thus far have been of the first two types. In hot water, alveolitis causing agents do not grow (8), but, especially, di- and polysaccharide-soiled evaporation and atomizing apparatus form good culture media for them (for instance, in printing factories) (9, 17). Apparatus not in use for some

time are especially dangerous (9, 16), as our case 1 indicates. In standing water the causative agents multiply better; the warmth of the motor even gives them a more physiological climate than normal indoor air — the optimal temperature for thermophilic actinomycetes being 45–55°C (20). Once the mold spores start to multiply, not even a thorough cleaning with a disinfectant is necessarily enough, as was true in our case 1; instead the apparatus must be sterilized in an autoclave before it can be used again (16). It is extremely important to clean humidifiers, for instance, with a 4% formalin solution, weekly (9) and change the filters often enough to avoid the dangers of contamination so that mold spores, bacteria or other organisms present or the occurrence of extrinsic allergic alveolitis will not cause a worsening of bronchial asthma (8) or result in bacterial infections, even fatal pseudomonas pneumonia, which has appeared in hospitals (6, 12). If the manufacturers provide effective directions for cleaning their product and these directions are strictly followed, all currently available humidifiers should be safe enough for use.

DISCUSSION

Thermoactinomyces vulgaris and *Microspora faeni* are the most common humidifier organisms to induce extrinsic allergic alveolitis (table 1) (1). In our first case there were precipitating antibodies against *Thermoactinomyces vulgaris* and in case 3 against *Aspergillus fumigatus*. Moreover the clinical symptoms always developed at a time when exposure to these microorganisms was probable. In such cases the diagnosis can be considered definite without the symptoms being provoked with the antigen concerned.

In the second case the etiologic agent remained unproved. In the literature such reactions have been connected with amoebas (9, 24), as was ours, or mold fungi (17). In addition cross-reactions have been found between mold fungi and actinomycetes antigens (5). Also thermotolerant bacteria

(11) and endotoxins may, because of indirect complement activation (19), be etiologic factors in the development of extrinsic allergic alveolitis or a similar febrile reaction.

In differential diagnostics, extrinsic allergic alveolitis should be kept in mind in all cases of recurrent fever, bronchitis and pneumonia, and also in cases of pulmonary fibrosis of unknown origin.

Before a diagnosis is made, and in acute cases, steroids can be used therapeutically to obtain a more rapid improvement in lung function (2, 4, 21).

The extrinsic allergic alveolitis caused by contaminated air-conditioning and humidification systems develops in four weeks to three years (table 1). In our case 1 the latency period from the beginning of exposure to the onset of symptoms was three to four months. The speed of development probably depends, at least partially, on the degree of exposure.

If the diagnosis is made and exposure is eliminated, prognosis is good. Lung function usually returns to normal in some days to a few weeks in acute cases (2, 4, 16) and in some months (2, 14, 21) to two years (13) in more chronic ones, such as our case 1. In the acute phase the disease can nevertheless be nearly fatal (13).

REFERENCES

1. BANASZAK, E. F., BARBORIAK, J., FINK, J., SCALON, G., SCHLUETER, D. P., SOSMAN, A., THIEDE, W. and UNGER, G. Epidemiologic studies relating to thermophilic fungi and hypersensitivity lung syndromes. *Am. rev. respir. dis.* 110 (1974) 585—591.
2. BANASZAK, E. F., THIEDE, W. H. and FINK, J. N. Hypersensitivity pneumonitis due to contamination of an air conditioner. *N. engl. j. med.* 283 (1970) 271—276.
3. BURKE, G. W., CARRINGTON, C. B., STRAUSS, R., FINK, J. N. and GAENS-LEER, E. A. Allergic alveolitis caused by home humidifiers. *J. am. med. assoc.* 238 (1977) 2705—2708.
4. FINK, J. N., BANASZAK, E. F., THIEDE, W. H. and BARBORIAK, J. J. Interstitial pneumonitis due to hypersensitivity to an organism contaminating a heating system. *Ann. intern. med.* 74 (1971) 80—83.
5. FLAHERTY, D. K., MURRAY, H. D. and REED, C. E. Cross reactions to antigens causing hypersensitivity pneumonitis. *J. allergy clin. immunol.* 53 (1974) 329.
6. GRIEBLE, H. G., COLTON, F. R. and BIRD, T. Fine particle humidifiers, source of *Pseudomonas* seruginosa infections in a respiratory-disease unit. *N. engl. j. med.* 282 (1970) 531—534.
7. HODGES, G. R., FINK, J. N. and SCHLUETER, D. P. Hypersensitivity pneumonitis caused by a contaminated cool-mist vaporizer. *Ann. intern. med.* 80 (1974) 501—504.
8. HÖCHLI, U. Luftbefeuchter und Bronchialasthma. *Praxis* 58 (1969) 954—956.
9. HOSCHEK, R. Kurzdauernde Gesundheitsstörungen durch Luftbefeuchter in graphischen Betrieben. *Zentralbl. Arbeitsmed. Arbeitsschutz* 2 (1972) 35—38.
10. KELLER, H., SPENGLER, H. and LATSCHA, U. Befeuchterfieber. *Schweiz. Med. Wochensh.* 102 (1972) 865—872.
11. KOHLER, P. and GROSS, G. Humidifier lung: Hypersensitivity pneumonitis related to thermotolerant bacterial aerosols. *Chest* 69 (1976): suppl. 2, 294—296.
12. LIEBETRAU, B., THIEM, A. and HANF, R. Raumluftbefeuchter als Quelle von Gesundheitsstörungen. *Z. Gesamte Hyg. Ihre Grenzgeb.* 1 (1974) 17—23.
13. MARINKOVICH, V. A. and HILL, A. Hypersensitivity alveolitis. *J. am. med. assoc.* 231 (1975) 944—947.
14. MILLER, M. M., PATTERSON, R., FINK, J. N. and ROBERTS, M. Chronic hypersensitivity lung disease with recurrent episodes of hypersensitivity pneumonitis due to a contaminated central humidifier. *Clin. allergy* 6 (1976) 451—462.
15. PEPYS, J. Hypersensitivity diseases of the lung due to fungi and organic dusts. In: *Monographs in allergy*. S. Karger AG, New York, N.Y. 1976, pp. 1—19.
16. PESTALOZZI, C. Febrile Gruppenerkrankungen in einer Modellschreinerei durch Inhalation von mit Schimmelpilzen kontaminiertem Befeuchterwasser. ("Befeuchterfieber") *Schweiz. Med. Wochensh.* 89 (1959) 710—713.
17. PICKERING, C. A. C., MOORE, W. K. S., LACEY, J., HOLFORD-STREVEIS, V. C. and PEPYS, J. Investigation of a respiratory disease associated with an air-conditioning system. *Clin. allergy* 6 (1976) 109—118.
18. REED, C. C., SOSMAN, A. and BARBEE, R. A. Pigeon breeders lung: A newly observed interstitial pulmonary disease. *J. am. med. assoc.* 193 (1965) 261—265.
19. RYLANDER, R., HAGLIND, P., LUNDHOLM, M., MATTSBY, I. and STENQVIST, K. Fever caused by a humidifier-endotoxin as a causative agent? *Läkartidningen* 74 (1977) 3739—3740.
20. SEABURY, J., SALVAGGIO, J., DOMER, J., FINK, J. and KAWAI, T. Characteriza-

- tion of thermophilic actinomycetes isolated from residential heating and humidification systems. *J. allergy clin. immunol.* 41 (1973) 161—173.
21. SWEET, L. C., ANDERSON, J. A., CALLIES, Q. C. and COATES, E. O. JR. Hypersensitivity pneumonitis related to a home furnace humidifier. *J. allergy clin. immunol.* 48 (1971) 171—178.
 22. TOURVILLE, D. R., WEISS, W. I., WERTLAKE, P. T. and LEUEDEMAN, G. M. Hypersensitivity pneumonitis due to contamination of a home humidifier. *J. allergy clin. immunol.* 49 (1972) 245—251.
 23. WEISS, N. S. and SOLEYMANI, Y. Hypersensitivity lung disease by contamination of an air-conditioning system. *Ann. allergy* 29 (1971) 154—156.
 24. ———. M.R.C. symposium: Humidifier fever. *Thorax* 32 (1977) 653—663.

Received for publication: 7 March 1978