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# MYCOTÓXINS AND EXHAUSTION SYNDROME IN A HOSPITAL

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## Abstract

After six years of research, studies and relentless struggles in the workplace, the staff at the Hôpital St-François d'Assise in Québec City finally succeeded in getting the hospital and its ventilating systems decontaminated. Hospital personnel had been coming down with exhaustion syndrome since 1982. At first they were thought to suffering from the effects of cytomegalovirus, viral mononucleosis, the Epstein-Barr virus or even "Mass Psychogenic Illness." Clinical examinations and lab results showed a lymphocyte imbalance and suggested that the neuro-vegetative system was affected. A massive health survey found 300 diagnosed cases, with more than 600 people possibly affected. The syndrome is associated with toxins from mould spores which proliferate in the hospital and its ventilating systems as a result of water leaking in through the roof and windows. At least two species of these moulds (Stachybotrys atra and Trichoderma viride), recognized for their immunosupressant and neurotoxic effects, produce mycotoxins.

## Key words

Mycotoxins. Stachybotrys atra. Trichoderma viride. Exhaustion syndrome. Stagnant water. Hospital. Mechanical ventilation.

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## INTRODUCTION

The quality of air indoors and outdoors is an increasingly vital public health issue. Current energy-saving policies, which consist basically in reducing the flow of fresh air, have so far only been linked to disconfort in hermetically sealed buildings whith mechanical ventilation. Our experience indicates, however, that when these policies are combined with inadequate maintenance, they can result in chemical and above all microbial contamination. We believe that our case study of Hôpital St-François d'Assise in Québec City sheds new light on the real sources of certain comtemporary health problems.

## SOME HISTORY

Hôpital St-François d'Assise (HSFA) is a general hospital with 836 beds and a staff of about 2.000 employees. The Hospital is spread out over four separate buildings (wings) all connected by tunnels or above-ground passageways.

In June 1982, the news media reported the emergence of symptoms of severe fatigue amoung some fifty Hospital employees. The Hospital's own microbiology department concluded that the cases were part of an epidemic of cytomegalovirus (CMV) in Québec City.[1]

For nearly two years the employees suffering from what was presumed to be CMV were regularly put on mandatory sick leave by the Hospital's health service. Since the desease is transmitted by direct human contact, Hospital management rejected accusations that the workplace was unsanitary. Confronted with the large number of cases, it claimed that it was probably a form of group hysteria (Mass Psychogenic Illness). Information sessions were held for the staff, at which it was recommended that they get some rest and go to bed earlier.

In August 1984, the Commission de la Santé et de la Sécurité du Travail du Québec (CSST: The Quebec occupational health and safety board) received an anonymous request for an investigation indicating that "Employees are suffering from cytomegalovirus and the problem has taken on epidemic proportions. All the employer is doing is granting up to three months of sick leave." The CSST turned to the regional Département de Santé Communautaire (DSC: community health department), requesting that it compile all the medical files of the employees affected at HSFA. The report two years later used medical files for a total of 116 employees affected. An analysis of how the diagnoses progressed over time indicated that cases of CMV had peaked in 1982, and then been replaced in 1983-84 by the Epstein-Barr virus (EBV) as the most frequently diagnosed problem.[2]

Meanwhile, an occupational health physician hired by the union examined a dozen patients and concluded that a new syndrom was involved. Given that the air indoors at the Hospital was the only possible common vector for all the persons affected, the physician recommended that the ventilating

systems be meticulously tested, looking in part for microbial contamination.[3]

A preliminary inspection by the Service du Génie Industriel de la CSN (SGI-CSN: industrial engineering department of union employees, the Confédération des Syndicats Nationaux) confirmed that there was stagnant water in the ventilating systems, and that an analysis of the microflora was needed.[4]

The CSST made a similar recommendation and presented the Hospital with a list of ten departures from standards involving the dirtiness and poor use of its ventilating systems. The CSST also raised a number of questions about the new energy-saving programme introduced by an engineering firm of energy specialists.[5]

As well, given that the Hospital is located close to the municipal incinerator and a large paper mill, the CSST recommended that the ventilating systems be cleaned with a desinfectant soap.[2]

Rather than accepting and complying with the remedial measures required, the Hospital spent several months in a legal challenge to the report. During the hearings, a microbiologist called as an expert witness by the Hospital testified that in her opinion, all the cases she had examined involved people worn out from too much time spent in discotheques rather suffering from serious illnesses![6]

## METHODOLOGY OF THE UNION INVESTIGATION

Fact-finding questionnaire. To determine the number of employees actually affected by symptoms of poor health or the syndrome, the union organized a vast investigation using a computerized questionnaire whith 42 questions. Employees work history was broken down by age, sex, general and departmental seniority, kinds and frequency of symptoms experienced, physician consulted and their diagnoses, treatment prescribed, occurence of the syndrome in the family, length and frequency of sick leave, smoking habits, etc.

The two main questions dealing symptoms covered 55 of the main symptoms associated with health problems in the "unhealthy buildings" and more specifically with the St-François d'Assise syndrome". A team of about twenty people was in charge of distributing the questionnaire in the workplace during 18 shifts.[7]

Investigation into the construction and subsequent history of the buildings and ventilating systems. The union's investigation sought to determine the source of the disease by piecing together the facts objectively. Reconstruting the history of how the buildings were built and their subsequent evolution included compiling information of the age of the buildings, the various repairs and renovation work carried out, employees' complaints about the environment, the use of pesticides inside buildings, etc. Data on the ventilating system covered the kinds of

ventilating systems (open or sealed windows, constant -or variable-flow equipment, energy-saving programmes), the frequency, methods and quality of maintenance (filters, fans, dampers, ducts...), the king of humidifier system (cold water or vapour), the chemical additives used, etc.

Microbiological analysis. On July 1, 1987, sterile swabs were used to take 33 samples wherever mould could be seen (windows, walls, stairwells, false ceilings, etc.) and in the main ventilating systems (intake and return air ducts, humidifier nozzles, filters, diffusers, grills). The samples were refrigerated immediately and kept in cold storage until they were incubated in the Laboratoire de Biotechnologie de l'Environnement (environmental biotechnology laboratory) at the Universaité du Québec à Montréal (UQAM).

Microbial analysis of the samples under the microscope established the inoculating dilutions according of the samples' degree of contamination. Micromycetes were isolated using three different culture media (Sabouraud, potato-dextrose-agar and cellulose Czapek). To slow down the growth of rapid strains and to prevent the development of bacteria, Rose Bengal and streptomycin were added to the media used. The number of colonies in each culture medium was counted. The strains isolated and identified were prepared for verification of the production by mycotoxins in vitro.[8]

A number of strains isolated and known for their toxicity were transferred to a nutrient medium favourable to the synthesis of trichothecenes (rice).

They were kept at 26°C for two weeks and then at 10°C for another two weeks to as to duplicate the optimal physical conditions for synthesizing mycotoxins. After the incubation period, the mycelium and the medium were homogenized in a 90% methanol solution. The filtrate of this homogenate was subjected to various extractive processes: a hexane wash, separation and chelating with a ferric colloid. The methanol was evaporated off the colourless filtrate and the aqueous solution left was mixed with dichloromethane and $Na_2SO_4$. Reduced to a few drops, the final solution was subjected to thin-layer chromatography on 60TLC silica gel plates. The diluant (5:1) was ethyl acetate-n hexane and developed in two stages with 4-(p-nitrobenzyl) pyridine (NBP) and tetraethylene pentamine (TEPA). Results were compared with the "standard kit" trichothecenes. The Rf values of the spots that emerged were measured on the developed chromatograms. Layers transferred to a cellulose medium were handled the same way.[9] [10]

In March 1988, an RCS-Biotest device wa used to take samples to test for airborne microflora.

Medical assessment. Summaries of files from the Hospital's health service as well as those provided by the unions were consulted, and 47 patients were examined. The usual biological tests were done: tests for liver functions, full blood counts, sedimentation rates, immuno-electrophoresis, quantitive analysis of anti-CMV and anti-EBV antibodies using immunofluorescence, toxoplasmosis, etc.[3]

Cytofluorimetry with monoclonal antibodies (EPIC-Coulter Co.) was used to obtain a listing of lymphocytes and the various sub-types (B,T,$T_{act}$, $T_{supp}$, NK).

## RESULTS

Fact-finding questionnaire. More than 70% of employees filled out and returned the questionnaire (1400/1940). Table 1 gives the results of a preliminary computerized compilation of symptoms, accurate to 95%.[11]

Table 1: Frequency of the various symptoms

| SYMPTOMS | PER CENTAGES |
|---|---|
| Dry lips | 62 |
| Dry skin | 58 |
| Having to go to bed much earlier than before | 58 |
| Exhaustion | 52 |
| Feel hot | 52 |
| Hawning | 49 |
| Headaches in front of head (forehead, ocular, temple) | 49 |
| Sleepiness | 46 |
| Muscle pains | 45 |
| Impatience (irritability) | 43 |
| Strong urge to sleep | 43 |
| Usual leisure activities harder to do | 42 |
| Frog in the throat | 40 |
| Air feels heavy | 38 |
| Perspiring quichly when effort is made | 37 |
| Sore throat | 36 |
| Rhinitis | 36 |
| Feeling cold | 36 |
| Difficultty with mental concentration | 35 |
| Irritated eyes | 34 |
| Repeated sneezing | 34 |
| Itching | 33 |
| Left breathless after effort | 31 |
| Insomnia | 30 |
| Dizzy spells | 28 |
| Dry cough | 27 |
| Memory loss | 27 |
| Repeated flu | 27 |
| Severe hunger | 27 |
| Depressed for no reason | 26 |
| Chills | 24 |
| Headaches in back of head (occipital) | 23 |
| Eyes feeling veiled | 23 |
| Sinusitis | 23 |
| Bone pains | 22 |
| Ganglions in neck and underarm swollen and/or painful to the touch | 22 |
| Substantial nocturnal perspiration | 21 |

Some 300 medical diagnoses related to monocucleosis, Epstein-Barr virus or cytomegalovirus were compiled.

A statistical analysis of work histories, diagnoses compiled and symptoms indicated that employees were affected irrespective of age, sex, general or departmental seniority, trade or occupation of place of work in the Hospital.

Investigation into the construction and subsequent history of the buildings and ventilating systems. The four wings of the Hospital were built at separate times - in 1914, 1947, 1959 and 1970. Wing A, a six-storey building, is the most recent built and the only one that is hermetically sealed with built-in ventilating, air conditioning and humidifier systems.

It is estimated that this wing cost more than CAN$10,000,000 to build. For reasons that remain unclear, it did not stand up well to the weather, and by 1972 there were already reports of water leaking in. The leaks were still occuring in 1974, when tey caused in considerable damage to the electrical system. The ensuing repairs apparently did not last any better, because by the winter of 1976 humidity has resulted in deplorable sanitary conditions and characteristic infestations of insect.

Bogged down in lawsuits brought to determine the builders' liability, the Hospital made do with makeshift solutions to catch the water leaking in. Instead of carrying out basic repairs, it installed leak collectors around windows in stairwells and in the false celings on the upper storeys (plenum chambers on return air ducts).[1]

Various repairs work was done over the years without any precautions being taken to prevent raising and displacing microflora inside the Hospital.

Assertions that the Hospital was not contaminated were based on scientifically worthless microbial analyses. The ventilating system was shut down whenever samples were tken. In fact, in one place the hot and cold air ducts were inhooked from the air chamber. No micro-organisms were identified.[12]

The constant-flow ventilating systems were replaced by variable-flow systems, mainly so that fresh air intake could be limited to 75% of moninal capacity. Throttles were installed on most of the air-feed fans to open and close when the fresh air intake dampers did in response to a computerized programme based on fluctuations in outdoor temperatures and indoor thermal loads. Operating hours for the various different ventilating systems (includind in surgery) were determined by a computer programme. The minimum quantity of fresh air was set at 2.5 litres/second/person (L/sec/person) in accordance with ASHRAE standard 62-1981.[13 14 15 16 17]

Microbiological analysis. Eleven (11) of the 33 samples taken had no mycrocycetes. Table 2 gives the species found.

Table 2: Species of micromycetes found

| | |
|---|---|
| Aspergillus niger (group) | Aspergillus versicolor (group) |
| Aspergillus fumigatus | Aspergillus niger |
| Common penicillium series | Penicillium sp.1 |
| Penicillium sp.2 | Penicillium sp.3 |
| Gliocladium sp. | Acremonium |
| Epicoccum sp. | Trichoderma viride |
| Alternaria alternata | Cladosporium sp. |
| Phoma sp. | Stachybotrys atra |
| Ulocladium sp. | |

All the strains of Stachybotrys atra and Trichoderma viride were mycotoxin producers. The Rf values of the trichothecene spots from Stachybotrys atra stains grown in both media (rice and cellulose) were identical (Rf: 0.20; 0.38; 0.50). The Trichoderma viride strains grown in the rice medium all produced trichothecene spots with constant Rf values (0.5; 0.76). The synthesis process gave the same results for a cellulose medium. Analyses using other methods of extraction seem to indicate that there are many other strains and species of mycetes that produce mycotoxins.[10 18]

With the RCS-Biotest samples, moulds (Stachybotrys atra and Trichoderma viride) were found on 4 of the 32 strips used.

Medical assessment. The clinical table indicated that there were certain symptoms cropped up regularly and repeatedly: intense fatigue, problems related to the central nervous system (problem with memory and intellectual concentration, irritability, insomnia, depression for no apparent reason, uncontrollable weeping), generalized muscular pain, more frequent infections of the upper respiratory tract, chronic throat irritations, occasional diarrhea, etc. The syndrome could last for one or many months, and symptoms gradually improved when the patient was away from work. A physical examination turned up painful cervical and axillary microadenopathies in about 2/3 of the cases examined.[3]

A number of cases showed signs that the neuro-vegetative system was affected. Psychiatric hypotheses were discarded after psychological testing produced normal results. Neither the medical histories nor the blood tests gave any hint of heavy metal poisoning or intoxication involving other chemical products such as pesticides.

Certainly there were some cases of CMV with very substantial increases in the level of antibodies. However, other cases were labelled CMV without any real proof, since the clinical evidence was not consistent with the symptoms usually described for healthy patients suffering from a cytomegalovirus infection.[18]

The average age of the victims (34 years old) cast serious doubts on the exact nature of the diagnoses of mononucleosis. Depending on the year (from 1980 to 1986), mononucleosis was diagnosed between 10 and 50 times as often as the rate at which it occurs in the population in general.

In the laboratory, the usual biological tests were unrevealing. However, the tests for immunological functions indicated that the total number of lymphocytes was down near the bottom of the normal range, a finding that was more pronounced in the case of lymphocyte sub-types (B, T, $T_{act}$, $T_{supp}$, NK). All the results pointed to the presence of a syndrome of lymphocytic "dysregulation".

As a final step, results were forwarded to two experienced researchers in this field who confirmed the plausibility of a syndrome of mycotoxic origin, although the hypothesis of a chemical intoxication was not excluded.[20 21 22 23 24 25]

Latter in the research process, blood samples and swabs of nose and throat secretions were taken from two different groups. The first group was drawn from employees affected by the St-François d'Assise syndrome; the second was a control group. The samples were sent to a laboratory for a comparative analysis with the mould specimens taken in the Hospital. There were no significal results.[26]

## DISCUSSION

Although a direct link between the presence of moulds in the workplace environment at the Hospital and the general health of employees has not been established beyond all doubt, it does seem to be the only plausible explanation until proof to the contrary. Samson[27] and Flanningan[28] have described a number of epidemics of intense fatigue in buildings contaminated by moulds.

Statistical results indicated that the diagnosis of "Mass Phychogenic Illness" was unfounded.

As for the ventilating system, our experience indicate that the timers and computers used to shut down ventilating systems outside of hours when a building is deemed occupied should be unhooked to ensure that there is an adequate minimum supply of fresh air at all times. Energy-saving programmes must be redesigned using criteria other than the reduction of the fresh air flow in response to outdoor thermal constraints and indoor loads (e.g. heat exchangers, opening and closing fresh air dampers on the basis of carbon dioxide concentrations, etc.).

Molina et al.[29] conclude that ventilating systems in a hospital should be treated as medical equipment. All sources of stagnant water must be eliminated immediately (drains maintained in all ventilating, air conditioning and humidifier equipment, sloping roofs, etc.).

To use of cellulose-based filters should be re-examined, as they may give rise of the production of mycotoxins. According to Miller et al., there is no acceptable level of Stachybotrys atra and intensive investigation should go on to determine if there is a cluster of microflora proliferation. In positive conclusion, decontamination should be starsted immediatly.[30 31]

Our experience taugh us that very few researchers in Québec are working in the field of microbiology applied to workplaces and ventilating systems, although these are sites of major microbial contamination.

In conclusion, the Hospital management's intransigent attitude and its disregard for its employees' health problems are throwbacks to another era. Unfortunately, a great deal of time and energy was wasted as a result. Similar attitudes are often found among building managers who refuse to take occupants' complaints seriously as a health issue and not merely one of comfort. At a recent conference on indoor air quality held in Montréal, all the participants in the plenary session concluded that it was necessary to give people raising complaints about air quality the benefit of the doubt and to investigate the seriousness of complaints with the help of a widely distributed questionnaire.[32]

Finally, following a meeting with the Ministère de la Santé et des Affaires Sociales in March 1988 and visits by inspectors specialized in assessing building quality, the Ministère autorized a budget of CAN$4.5 millions to repair and decontaminate Wing A of the Hospital and its ventilating systems.

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