THE CASE OF THE INTOXICATED CELLS—AN EPIDEMIOLOGIC NOTE

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An episode is described in which tissue culture in a laboratory could have become intoxicated due to the recirculation of toxic exhaust fumes extruded from the roof of a research institution. A route of entry was found whereby a portion of fume hood exhaust was reintroduced into the building by means of large intake fans located on the roof near the exhaust ducts used to cool the elevator cables and motors at the top of the elevator shafts. The descending action of the elevator created a suction which pulled the polluted air down the elevator shafts and into the corridors. Such mechanisms for cooling elevator shafts are widely used in the modern architecture of commercial, industrial and laboratory buildings, and they should therefore be considered in epidemiologic investigations of airborne infections or intoxications of undetermined origin.

air pollution; architecture; environmental exposure; environmental health; laboratories; tissue culture; toxicology

The relationship between occupational exposure to environmental hazards and health risks has been the basis not only for the field of occupational and industrial health but for the entire field of environmental health studies. The results of high exposure to physical, chemical or biologic substances in the industrial plant have long proven to be the useful starting point for laboratory experiments leading to the establishment of acceptable standards of minimal exposure. However, that the

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buildings in which these laboratory experiments are performed may also be the source of occupational exposures due to faulty building design or operating deficiencies has not been as widely appreciated.

It is the purpose of this note to report an observation at the National Institutes of Health (NIH) which illustrates how an air flow design deficiency within a building design may serve as a contributory factor in causing area contamination. This design feature should not be overlooked in investigations for the source of cases involving aerosol exposure to chemical, physical or biologic agents in a particular building structure. Air handling systems have become of great interest in recent years as a result of the Legionnaire's disease outbreaks and their relation to building design features (1).

MATERIALS AND METHODS

In July, 1976, an episode was investigated which involved the failure of several cell culture systems in a block of
laboratories in Building 37 of the National Cancer Institute, NIH, in Bethesda, Maryland. The initial complaint of failure of normal cell growth tissue cultures was common enough to laboratories working with cell culture systems. However, the incident had gone on for an inordinate length of time and did not seem likely, as is usually the case, to cure itself despite all efforts on the part of the experienced research staff.

The problem had started one and a half years earlier in a group of laboratories which used cloned cell lines and primary tissue cultures for the testing of chemical mutagens and carcinogens. The chemical agents were added to the cell cultures which were examined daily for the effects. Four laboratories located as a group in a peripheral corridor of the building were involved. The laboratory group had been in existence for seven years and, until this particular episode, the research systems experienced only the usual temporary difficulties normal to such operations.

In the winter of 1974–1975 one laboratory started to experience unusual difficulties. The cells became “sick,” but did not die. They developed an unusual appearance and did not respond typically to exposure with known chemical agents as they had in the past. Their behavior was erratic and experiments which worked one day could not be duplicated the next. The changes were subtle and apparent only to the group of investigators working with the cells. The investigators described the cells as “intoxicated.” A few months after the onset of difficulties in the first laboratory, another laboratory in the same wing began to experience similar problems, although these investigators were not working with the same cell lines. A different room and staff were involved, but there was some overlap in media, supplies, and plastic or glassware. Within the next few months all the laboratories in that group became involved, a total of four. As is usual in such cases, the investigators changed media, glassware, reagents, etc., all to no avail. They cultured for microbial contaminants with negative results.

The group considered that the ambient air might be involved. In March, 1976, one experiment by the laboratory group was undertaken to grow the cells in another building (Building 13). The cells grew normally, but for various reasons the experiment was not duplicated in Building 37 at the same time. Therefore, a firm conclusion could not be derived from this uncontrolled experiment. Nevertheless, the results were enough to lend support to the possibility that the problem was one of air pollution.

This suspicion was expressed to the engineering staff of the NIH complex. Building 37 had been specifically designed to undertake the kind of research performed by the affected laboratory group and unless some defect could be detected in the design or operation of the physical plant it was deemed unlikely that the building’s air circulation system could be involved.

In March and May, 1976, at the initiative of the laboratory group’s director, an air sampling was made in the laboratories and corridor of the affected group. Abnormalities were found in the unexpected presence of chemical residues which had no reason to be in that corridor since they were not used by the adjoining laboratories. In May, the NIH engineers performed an operating survey of the building with particular attention to the air flow system. The engineers found that basically the air circulating system was operating as designed with minor variations caused by the manipulation of the air flow systems within laboratories and offices by the building’s occupants.

Nevertheless, it was decided to undertake smoke bomb studies on the roof to detect if atmospheric flows and inversions were producing reintroduction of chemicals emitted into the ambient air from exhaust stacks on the roof into the air in-
take system located in the basement. Simultaneously, a controlled study was performed to grow the cells in Building 37 and in a control laboratory in Baltimore by the same researcher using the same cells, media and plastics, and varying only in the ambient air. Laboratory procedures were observed for possible procedural defects and the hypothesis was examined that there was a defect in the design of the mechanical systems within the building.

**Results**

An examination of the various cell cultures revealed that the cells all behaved similarly despite differences in their origin, variations in the media used and the personnel and staff working with them. Some other laboratories in the building noted similar behavior of their cells but not as long lasting in duration. The cells did not die and fall off the glass as is typical with many of the laboratory intoxications noted in cell culture operations. A single condition apparently was responsible, and it was apparently a new phenomenon for that laboratory group, extending over a two-year period of time. An examination of laboratory procedures found a small number of technical procedural deficiencies, none of which could account for the distribution of the problem in time and place. The correction did not lead to any appreciable amelioration of the problem. However, the controlled experiment performed simultaneously in Building 37 and in the Baltimore laboratory did implicate ambient air as the probable source of intoxication for the cells. A closer examination of the building was therefore undertaken to search for defects in systems design or operation.

Building 37 is located on the western fringes of the NIH campus at Bethesda. The building itself is, with its basement, a seven-story, rectangular structure with 5365 square meters per floor. The building is designed so that there are extensive filtered air intake systems in the basement and an exhaust system on the roof. The roof has several penthouse-type enclosure structures on it which allow for maintenance of exhaust stacks. The stacks emerge almost flush with the tops of these penthouse-like structures. Two elevator shaft enclosures are located on the southeastern and northeastern corners of the roof. Each floor has peripheral corridors which completely enclose the four sides of the buildings. The outside wall of each peripheral corridor is, for the most part, a series of large window areas. There are also on each floor three internal corridors and four narrow service corridors for maintenance of the building infrastructure. These internal corridors run from east to west.

An exhaust system was designed to serve the chemical fume hoods of approximately 50 per cent of the laboratories. This system, however, was not working to capacity. Some hoods had marginal flow characteristics. But this situation could not explain the observed phenomenon involving the intoxicated cells. One had to account for a routine method of reintroduction of the fumes into the building involving only the last two years and then account for some reason why the four particular laboratories were getting an apparently greater exposure. The solution was found in a series of events starting with the release of a smoke bomb on the roof.

These studies revealed that not all of the effluent immediately escaped the roof but eddied, trapped in part between the penthouse-like structures on the roof. The question was raised as to whether there existed some possible intake for the effluent on the roof. Days were spent unsuccessfully searching for this intake until the location on the roof of two large intake fans used to cool the elevator equipment, such as friction cables and
motors, in the two elevator shafts. These fans were perfectly positioned in a cul-de-sac on the roof where effluent air coming from some of the exhaust stacks was trapped. The giant suction fans' ducts carried contaminated effluent into the elevator shaft where the rapid downward descent of the elevator produced a vacuum sucking the contaminated air down the shaft and into the peripheral corridors when the doors were opened. An inspection of the roof showed that in fact one could get gassed by exhaust fumes when standing by the appropriate sections of the roof near the powerful intake fans which were indeed sucking in the exhaust effluent.

The air circulation normally operating in the four peripheral corridors is dependent on conditioned air from the main supply system and supported by local recirculating units for cooling. These units were cut off approximately two years beforehand to conserve energy. In addition, at that same time, the building's peripheral corridors were made positive in pressure in relation to directly connecting laboratories, neutral in pressure to each other and subject to influx of air from areas of occasional higher pressures, such as stairwells and elevator shafts. Thus, the corridors could become collecting areas for that portion of the contaminated exhaust emitted from the hoods, and the contaminated air could be sucked down the elevator shafts and into the peripheral corridors where it could be introduced into the adjoining laboratories by positive pressure.

Several steps were taken simultaneously and in short sequence to eliminate the possible influx of contaminated air into the peripheral corridors. The fans serving the elevator machinery were reversed to discharge air to the outside and to bring cooling air into the mechanical room from the elevator shafts. Exhaust systems of the hoods and on the roofs were increased in capacity to improve the clearing of contaminated air from the building. The potential route of contamination from the stairwell was blocked by keeping the doors to the roof closed at all times. At the same time, a resolute and continuing decontamination effort in the affected laboratories was established to eliminate residual contaminants. These measures did not result in the elimination of the intoxicated cells problem, although some improvement in the affected cell systems was observed. However, the investigation uncovered a route of entry whereby released contaminants could be reintroduced into the building environment. Thus, a potential for contamination which could have an adverse effect on the cell system was found to exist.

**Discussion**

This investigation revealed a unique mechanism for contamination which could occur via elevator shafts and their intake equipment cooling fans. Such ventilation systems exist in the design of many different types of buildings and may play a role in a variety of building self-pollution problems, i.e., by building heating fuels, by chemical fume hood exhausts, and by biologic agents such as the one that causes Legionnaire's disease. The investigation illustrated the value of an epidemiologist in finding a solution to an environmental health problem and, thus, the importance of epidemiologic training for those persons who will be assigned to monitor occupational and environmental health and safety.

**Reference**