Harvard Public Health NOW

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TB Research Facility Is Proving Useful in Fight against Bioterrorism


Melvin First in front of "Building Five"

Situated on the flat roof of SPH-II is a pitched-roof, white building–about the size of an interstate freight trailer–where research is being done that may help scientists fight bioterrorism. The building wasn't constructed with bioterrorism research in mind. It was made to study tuberculosis. But the building's set-up may prove to be a perfect place to research ways to kill life-threatening agents using the power of ultraviolet light and of alternative methods of eliminating bioaerosols.

Ultraviolet is an energy wave and is not part of the visible light spectrum.

Colloquially known as "Building Five," the facility was designed and is run by Melvin First, professor emeritus of environmental health engineering in the Department of Environmental Health, and his HSPH colleagues Edward Nardell, Steven Rudnick and Thomas Dumyahn.

The facility consists of an exposure chamber the size of a large room and of a smaller anteroom. The chamber is largely empty save for ultraviolet light fixtures, monitoring equipment, small intake pipes and valves. But the emptiness belies the true subject of the scientists' attention–the air, or more specifically, the interaction between particles floating in the air and the ultraviolet light.

Inside the adjacent anteroom, researchers can control factors such as light intensity, ventilation, temperature and humidity. They can pump into the room, via a nebulizer and delivery tube, specific amounts of an organism to be studied. A bioaerosol generator is able to disperse particles in patterns, such as mimicking how particles would scatter if someone sneezed.

"The facility is unique because you can do biological aerosol studies in a chamber the size of a room while controlling factors such as room temperature, humidity and air exchange rates," said Professor First. Other chambers used for such work are usually much smaller and do not offer such a realistic opportunity to see how particles will behave in a life-sized room.

The agents currently studied in the facility are non-infective, but Professor First said that infective agents could be studied with modifications made to the building and with approval from Harvard's biological safety committee.

Professor First arranged for construction of the facility with the aid and active participation of Dean Paul Riccardi and his staff in 1998 and with a gift of an HVAC package by United Technologies' Carrier Corporation. The facility has been evolving ever since.

A spike in tuberculosis cases in the United States in the '80s had caused concern and had resulted in part from increasing numbers of people becoming ill with *Mycobacterium tuberculosis* resistant to multiple drugs. Adding to the problem was that the number of people with HIV, and thus compromised immune systems, had increased and had provided a vulnerable population for tuberculosis, said Professor First.

It has been demonstrated in laboratory studies that ultraviolet light can disrupt the DNA of *Mycobacterium tuberculosis*, killing the bacteria. William Wells, a professor at HSPH in the 1930s and '40s, recognized early on that ultraviolet light could be used to irradiate and kill airborne pathogens. After moving to Johns Hopkins University, Wells and colleague Richard Riley proved that tuberculosis was an airborne infection and conducted research that indicated ultraviolet light may disrupt tuberculosis transmission.

Study of ultraviolet light and tuberculosis diminished after antibiotics proved to be a powerful weapon against the disease, until the spike in US cases. Since then, Professor First has become a researcher in an ongoing series of double-blinded, controlled experiments comparing the incidence of tuberculosis infection in US homeless shelters, with some shelters having active ultraviolet light fixtures and others having lights that do not emit ultraviolet light. (See sidebar below.)

The tuberculosis study also is testing how different ultraviolet light fixtures work and how their ability to kill *Mycobacterium* *tuberculosis* is influenced by factors such as room ventilation and humidity. That’s where Professor First’s work plays a key role. In "Building Five," he is measuring how much radiant energy certain ultraviolet light fixtures emit over a specific area. He also is trying to determine the best way to irradiate particles with ultraviolet light without causing health problems to humans who may be exposed to the light as well. If accepted as safe and effective, ultraviolet light fixtures could be installed in hospitals, schools and offices to cut down on airborne infections.

There are three "zones" of ultraviolet light defined by their wavelengths. The kind that Professor First works with, UV-c, is not known to cause cancer or severe sunburns. It does not penetrate past dead cell layers of the skin, but it has been known to cause eye irritations. Placement of ultraviolet light fixtures, therefore, is important.

"You have to be careful about the amount of ultraviolet light that gets to the lower part of the room where the people would be," said Professor First. "You need to confine the ultraviolet light to a horizontal layer near the ceiling."

As part of the tuberculosis experiments, Professor First has been spraying a surrogate for *Mycobacterium tuberculosis* called Bacillus Calmette-Gúerin (BCG), a non-infective tuberculosis vaccine, into the exposure chamber of "Building Five" to see how it interacts with ultraviolet light.

Now, he is using the same experimental model to help fight bioterrorism.

"Ultraviolet light technology has become very interesting now that people are worried about bioterrorism," said Professor First. "This is why we’ve suddenly become very popular."

Professor First already is using a non-infective surrogate for anthrax spores to study the potential effects of ultraviolet light on the spread of anthrax and is gearing up to do similar research using a non-infective surrogate for smallpox.

"Most of our modeling has been done with tuberculosis, but there’s no reason to think that other organisms would behave any differently, other than in their susceptibility to ultraviolet light," said Professor First.

Both *Mycobacterium tuberculosis* and anthrax spores are highly resistant to ultraviolet light, making First’s research with BCG nicely applicable to anthrax-related studies.

He said, "As far as bioterrorism with anthrax or smallpox is concerned, what's important is how fast you can get rid of the stuff before people become infected."

Flooding the upper areas of rooms with ultraviolet light is one way being examined to possibly combat the agents. Another is to install ultraviolet lights in air ducts, which has the added attractiveness of not exposing peoples' eyes to UV-c.

Professor First received emeritus status at Harvard 21 years ago, but he has continued to work in the same office in Building I that he has occupied since 1961. He is pleased that his research in industrial hygiene and in biological aerosols has proven applicable in new ways.

"I have been working to expand the scope of respiratory diseases in addition to tuberculosis that we study because tuberculosis rates in the US have gone down, and there are other good areas to investigate," said Professor First.

Study in Homeless Shelters Investigates Power of Ultraviolet Light to Fight Tuberculosis

After tuberculosis rates began increasing in the US, Philip Brickner, chairman of the Department of Community Medicine at St. Vincent's Hospital and Medical Center of New York, asked Edward Nardell, associate professor in the Departments of Environmental Health and Immunology and Infectious Diseases, and Jonathan Freeman, then assistant professor in the Department of Epidemiology, if they wanted to conduct a study about the use of ultraviolet light to prevent tuberculosis transmission. Melvin First came on board as well. (See article above.)

The study has been ongoing for several years and involves 12 homeless shelters in New York City, New Orleans, Birmingham and Houston. A 13th shelter is expected to begin participation soon. At least two shelters in each of the cities are participating in the study, with one shelter serving as a control and the other serving as the site of an intervention. Each shelter has been equipped with special lights that illuminate the upper parts of rooms. In some shelters, the light is ultraviolet. In others, the light is a placebo, emitting a blue glow but not ultraviolet light.

While laboratory experiments have shown that ultraviolet light can kill aerosolized *Mycobacterium tuberculosis*, no study has yet shown that use of ultraviolet light would be practical in buildings. Factors such as light not reaching around corners and people turning lights off may limit the feasibility of ultraviolet light use, said Megan Murray, an assistant professor in the Department of Epidemiology who undertook the epidemiological arm of the study after Jonathan Freeman died in 2000.

A major goal of the research is to see if people in homeless shelters that use upper-room ultraviolet lights are less likely to become infected with tuberculosis than people who stay in homeless shelters without ultraviolet lights. Most tuberculosis infections do not result in disease, explained Murray. People who are infected with latent tuberculosis do not feel sick or have any symptoms, and they cannot spread tuberculosis. They may later develop full-blown tuberculosis disease, which is communicable. The study's scientists are not measuring cases of disease. They are measuring rates of new infections.

The study involves volunteers who have been informed of the research, its intent and their rights as research subjects. All study volunteers have tested negative on skin tuberculin tests before enrollment.

Homeless shelters were chosen as the sites for the study because of several factors. Brickner, who came up with the idea for the study, is an expert on health issues and the homeless. As a population, the homeless are at higher risk for tuberculosis infection than average Americans. Communal dining halls, sleeping facilities and other factors lend themselves to increasing the transmission rate of *Mycobacterium tuberculosis*. Also, the homeless shelters in the study provide health care to their residents so health care professionals are already on site.

Tuberculosis rates in the US have declined since the spike in the 1980s but remain a concern. The disease, particularly in its multiple drug-resistant form, is also causing problems for other nations where transmission is on the rise.

Because the study is blinded, the epidemiologists and clinicians do not know yet if the interventions with ultraviolet light are working. Preliminary data indicate that the conversion rate–the number of study participants who test positive on a tuberculin skin test but who may not yet have developed the disease–is about two to three percent, which is similar to rates in developing countries.

"Tuberculosis is an enormously important health problem, particularly in our homeless, prison and disadvantaged populations," said Murray. "The rise of multiple drug-resistant tuberculosis means that the disease is difficult to treat, sometimes impossible to treat. We need to reduce transmission of the bacteria. Right now, there aren't too many options. The bacteria are spread through the air. It's not like STDs, where you can tell people to abstain, however ineffective that may be. People have to breathe. If ultraviolet light does decrease transmission, it will be a good resource. We hope it will be one route to decrease transmission."

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