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'Electronic nose' could detect TB by sniffing patient's breath

New device undergoing sensitivity training

No matter how keen your sense of smell, it's a good bet you can't detect TB on a patient's breath. Someday in the not-too-distant future, an "electronic nose" being developed at the Illinois Institute of Technology in Chicago may be able to do just that.

The electronic nose spends its days sniffing mostly harmless varieties of bacteria in the laboratory of **Joseph Stetter**, PhD, laboratory chief at the chemical, biological, and physical sciences department at the university. The nose isn't much to look at, adds Stetter's colleague, senior research associate **Bill Penrose**, PhD. In fact, it's "kind of ugly," Penrose says, explaining that it consists basically of a bench-size collection of parts that includes a computer hooked to a box filled with electronic sensors.

Looks aren't everything, though. Working with TB isolates from the state TB lab in Chicago, Penrose has put the new device to the test. Of 24 lab samples, it has identified the 18 that were positive for *M. tuberculosis* and the six that were negative.

When the experiment was repeated a second time, the nose got all the answers right again.

A sensitive nose knows more

Like many a parent who envisions a big future for his brainchild, Penrose still isn't content. He wants the device to be more sensitive. "The key is not being able to distinguish one kind of bacteria from another, because we already know it can do that. What we want is for it to be able to distinguish bacteria at the very low levels you'd find in a medical situation," he says. "A breath test would be the brass ring. We'll really have accomplished something if you could just

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COMING IN FUTURE ISSUES

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- More good news about rifapentine
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breathe into a machine, and we could tell you if you have TB or not." Even if the nose never meets that expectation, it could still dramatically shorten time to diagnosis by conventional methods, Penrose adds.

Just as with human noses, the sensors that Stetter and Penrose's electronic nose uses produce a characteristic set of responses. If graphed, the responses make up what could be called olfactory fingerprints, each one unique.

Technology is rather simple

The concept of a breath test for TB isn't as far-fetched as it might sound. Many health care providers have whiffed the distinctive odor of ketones on the breath of a person with diabetes. Using the same technology, another group of researchers has managed to sniff out pneumonia, Penrose says. All the patients were intubated.

If Penrose succeeds in increasing his device's sensitivity sufficiently, the implications for TB diagnostics will no doubt be wide-reaching. Plus, because the technology involved isn't especially complicated, manufacturing such a device shouldn't prove to be difficult or costly. "The undergraduate student across the hall just made one that works," he says. "That was basically working from spare parts. It's not as if you need a micro-fabrication unit to make one of these things."

If a cheap, smart nose could be built, such a device would have special value in the Third World. "If we could pull that off, it would be a double brass ring," he says.

The nose works in much the same way as its flesh-and-blood counterpart. "We used to joke about it being an 'electronic nose,' but one day somebody pointed out that's exactly what it is — it works basically the same way as the human olfactory system," says Penrose.

People have about 100 types of receptors in their olfactory epithelium yet can distinguish thousands of odors. That's because each sensor produces its own characteristic reaction to an odor. Likewise, a given chemical sensor doesn't respond in the same way to one substance but reacts in an idiosyncratic fashion. "So if you put two, three, or four sensors together and expose them to a solvent vapor, each one will respond in its own way," he says.

Electronic noses already are being used by the food and beverage industries to sort out complex

bouquets of odorous components. A few years ago, scientists in Penrose's lab taught their device to distinguish sour or moldy batches of grain from good grain, a feat that had eluded government scientists using high-powered chemical methods.

So when will TB docs be able to order their own TB breathalyzers? "It's reasonable to think we'll be in pre-clinical within a year," Penrose says. The device has attracted a fair amount of outside interest, he admits, though not anything he can talk about yet.

When asked the other obvious question — what does TB smell like? — Penrose chuckles. "I don't know," he admits. "We did some tests a few years back with *E. coli* and other coliform bacteria. As any microbiologist well knows, you can tell them quite easily apart."

The same probably goes for TB in high enough concentrations, since researchers working with petri plates and deep cultures have been able to discern many kinds of bacteria from one another, both at the genus and species level. ■

Bill Gates donates $25M to TB's new drug group

Gift proves TB advocates are educating public

The Global Alliance for TB Drug Development, not even a year old, received a birthday gift in March from Microsoft chairman Bill Gates. Gates celebrated this year's World TB Day by handing the alliance a check for $25 million.

Because it's still in the process of incorporating as a nonprofit, the new organization doesn't even have a bank account where it can stash the money. And no one knows yet exactly what will be done with the gift because the person charged with writing a business plan for the foundation — **Carol Nacy**, PhD, the street-smart scientist who presides at Sequella Global TB Foundation in Rockville, MD — was still fretting over the first draft at press time.

None of that appears to ruffle Gates, however. "TB is a good example of how if we don't pay attention to these diseases, we'll go backward," he was quoted as saying.

To Nacy, the big question now is whether the new alliance will look and act like a business, an advocacy agency, a funding entity, or something else. "It's like, 'OK, folks, what do you want this alliance to be when it grows up?'"

Meanwhile, Gates' magnanimity offers heartening evidence that TB advocates are finally making a dent in public awareness, others say. "When we started in the fall, TB drug development wasn't part of the international agenda and hadn't been for over a decade," says **Ariel Pablos-Mendez**, MD, MPH, scientific adviser to the Rockefeller Foundation in New York City and the spearhead behind formation of the new alliance, which seems to have gotten TB drug development off the table and breathing again. "Now governments are geared up. Donors are geared up. Agencies are geared up. And more opportunity will be coming our way."

"To put together a group and have it get funding so quickly is really very encouraging."

Others are equally upbeat. "To put together a group and have it get funding so quickly is really very encouraging," says **Jim Yong Kim**, MD, director of the program of infectious disease at Harvard Medical School in Boston. "It shows how one foundation can alter the vision of the entire public health community. What if an even larger percent of all the ridiculously wealthy people in the world got interested in public health? I think you'd see a fundamental shift."

Part of the effect of Gates' gift is to shift thinking away from the "minimalist approach" Kim says has plagued public health thinking for so long. "That approach assumed public health budgets would always be very limited and that the most you could hope for would be a single, cost-effective strategy," he explains. "With this gift, Gates is essentially asking *why?* And I think he's exactly right."

Kim and others, Pablos-Mendez among them, say policy-makers' blinkered commitment to pushing the World Health Organization's approved strategy for TB treatment — directly observed therapy, short-course, or DOTS — has inadvertently caused some of the problem.

"WHO has tried very hard to implement DOTS, and of course that's been the right thing," Pablos-Mendez says. "But after a decade of trying to implement DOTS and finding that we're only at 25%, we see that DOTS alone is not enough. What we need is a new drug to simplify treatment."

At OSHA, it's a wrap; draft off for review

Publication likely by early summer

Only one hurdle remains before the new federal TB standard becomes law. The draft of the new rule has been handed over for review to the Office of Management and Budget (OMB), says **Amanda Edens**, MPH, project officer for the TB rule at the Occupational Safety and Health Administration (OSHA). The draft rule's stop at the OMB could take anywhere from one to three months, says Edens, because the office has up to 90 days to complete its task.

The draft rule is still on course for an early summer publication, she says, but the timetable depends on factors that are hard to predict. OMB "has a lot of other rules," she points out. "Frankly, I don't how important this one is to them. Big rules like ergonomics tend to take a lot longer compared to a rule like TB."

Once OMB hands the draft back to OSHA, any suggested changes may be incorporated. Then it's off for the final step — to Secretary of Labor Alexis Herman for a signature.

The new rule will become effective 30 days from whenever it's published in the *Federal Register*. "In effect, that's to give you 30 days to read it," Edens says. Even so, parts of the rule kick in on a graduated scale, as is explained in the rule section titled "Dates." The graduated sequence of events spelled out takes into account the fact that facilities need time to complete risk assessments, do skin testing, carry out training, and make structural changes to the building, if needed. ■

By April 18, alliance stakeholders were to have met in New York City to hash out business plan details, says Pablos-Mendez. Those on hand were to have included a representative of the Bill and Melinda Gates Foundation as well as other potential donors, plus virtually every major public health agency and nongovernment organization with an interest in TB.

At a meeting in Capetown, South Africa, earlier this year, those stakeholders set a goal of seven to eight years to find a drug that will shorten therapy to less than three months. Some candidates on the scene, though they don't seem likely to meet that goal, still might improve TB treatment, says Pablos-Mendez. Some are derivatives of other drugs; for example, Pathogenesis PA 824, which is a rifamycin derivative like rifapentene.

Other candidates are drugs already approved for other indications that look as if they also might have activity against TB. A fluroquinalone, moxifloxacin, is one such example, says Pablos-Mendez.

Still other candidates developed by using findings from exciting new genomic research have yet to emerge. That's the group to watch most closely, he adds. ■

On reportable infection, a frisky debate goes on

No way in Texas, but possibly in Mississippi

Last month's story about the policy of making TB infection reportable — an unusual practice, but one that's much admired in the few jurisdictions where it's practiced — caught *TB Monitor* readers' attention and drew a volley of responses.

When the state of Texas mandated the reporting of TB infection in children, the move turned out to be "an unmitigated disaster," says **Jeff Starke**, MD, chief of pediatrics at Ben Taub General Hospital in Houston.

"They didn't really publicize it, so people didn't know they were supposed to do it." But having done so probably wouldn't have made that much difference, he adds. "We all know that anything that depends on reporting by physicians is doomed to failure."

In Mississippi, on the other hand, state TB control officer **Mike Holcombe**, MPA, says the state's new policy of mandatory infection reporting — again limited to kids — may be giving TB controllers a leg up. The policy, inaugurated last October, mandates reporting of children ages 15 and under.

Holcombe says he can recall at least one instance in which a child's positive skin test otherwise might not have been reported. Plus, an associate investigation of the child's contacts led

to the case that presumably had infected the child.

That illustrates the double usefulness of the policy, he adds. "First, we're making sure children get appropriate preventive therapy. And second, because we view infections among children as sentinel events, we use the report as an opportunity to look for the source case."

Starke says he doesn't think the second rationale counts for much because, in his view, associate investigations are often a wasted effort. "A lot of times, the skin test you're working from is a false-positive," he says. "I'd rather talk about my two favorite activities, which are contact investigations and screening at-risk populations. That's a better use of resources."

Tests may not be reliable, cost-effective

But what about infection reporting as an epidemiological tool? Starke still isn't convinced because in the low-prevalence areas where reporting positive tests is doable, many positive skin tests are actually false. Spot surveys of tuberculin reactivity would be much better to get a sense of infection rates among various groups, he suggests.

Kimberly Fields, RN, chief of the TB control program in Washington state, also gives a thumbs-down to the policy, which Pierce County recently enacted for all ages. Because the state has a decentralized public health structure, Pierce County can certainly do as it likes, Fields adds, and she says it will be interesting to see how the new policy plays out.

For the moment, she's skeptical. "Infection reporting is very resource-intensive. Someone has to be available to interpret the data and then probably to re-enter it. That all takes time and resources at a time when federal dollars are down." ■

Correction

In last month's story on reportable TB infection, Heather Duncan, senior health policy analyst for Florida's TB and refugee health program, was misquoted. Her statement should have read, "Tens of thousands of people with TB infections are found every year." ■

Mormon missionaries educated on TB threat

Church policy on testing is strengthened

Since its founding in 1830, the Church of Jesus Christ of Latter-day Saints, whose followers are commonly known as Mormons, has placed its young missionaries in every corner of the globe. With TB rates high in many of the countries where those missionaries serve, Utah TB controllers have been asking the church to work harder at making its young people aware of the risks.

"There is the potential for a problem," says **Teresa Garrett**, RN, MSN, head of Utah's TB control program in Salt Lake City and director of the state's refugee health program. "Anytime you go to a country where TB is [an] epidemic for an extended period of time, you need to get tested for TB upon your return." For the last year, state TB controllers have been working with the church to provide education and help develop policies, Garrett says. "We believe the church has a responsibility to provide that education [to missionaries], and, to their credit, the church agrees."

Reports of illness not unusual

The LDS church, as the entity is known in Utah, has a longstanding TB policy that encourages returning missionaries to be tested for TB. The problem is that until recently, enforcement has been minimal. "In the last year, church leaders have begun to talk more about the policy and to work harder at enforcing it," Garrett adds.

Mostly because infection isn't a reportable condition in the state, TB controllers don't know how many returning missionaries are infected with TB or how many go for the skin test upon returning home, she notes.

Clifton Harris, MD, chairman of the Medical Services Commission of the missionary department of the church, says the data aren't tracked by the church, but he guesses the rate of conversion among returning missionaries is 1% to 2%. Whatever the rate, reports of sickness among returning missionaries don't seem to be especially unusual.

Rebecca Reese, RN, a nurse consultant to the state TB program and a member of LDS, says when her son returned from a two-year stint in

the Dominican Republic, he had dengue fever "and several other things." Fortunately, TB or TB infection weren't among them. "He looked terrible when we first saw him," she remembers. "They pick up all sorts of things."

Many go to Latin America or Asia

At present, about 60,000 Mormons are engaged in mission work, says Harris. About two-thirds of them serve outside the United States, he adds. Top destinations include Latin America, Asia, and Africa, Harris says. Russia, the Pacific Islands, Taiwan, and Hong Kong run close behind.

Even when the missionaries serve stateside, church members say, they frequently land in postings where TB rates are high. For example, a family Reese knows sent its son to live with a community of Hmong refugees in Chicago.

In host countries, missionaries divide their time between Bible study and proselytizing. They also devote a day a week to community service projects, like digging latrines or working in day care centers. Harris says he's not sure how many young men and women do mission work. Church members say the percentage is high, with men much more likely to serve than women. According to church tradition, young men who feel they've been called to do mission service can begin at age 19; women must wait until they're 21. Men serve for two years; women for a year and a half.

Utah TB controllers emphasize they aren't singling out Mormons for special attention or criticism. "We're reaching out to all international travelers, from Presbyterians who do missionary work for their church to people who go to Africa to work in a medical clinic to volunteers who go work with Habitat for Humanity," says Garrett.

Even so, some church members are uncomfortable with the topic. Harris suggests that foreign-born residents of the United States, not missionaries, pose the real danger. "We've got a lot of foreigners coming in, and they're inundating us with TB," he says. "We've got Russians, Filipinos, Laotians, and Vietnamese, not to mention all the Mexicans who swim the river. And they're all bringing resistant organisms with them."

The state has started looking at members of the church because in other respects, Utah's TB rates are extremely low, says Garrett.

"We had only 40 cases last year, and our incidence rate was 1.9," she says. "We're closing in on elimination. That's why it's time to turn our attention to this." ■

Thalidomide's promise provides a double bonus

May decrease symptoms as it speeds cure

In a research lab at Rockefeller University in New York City, an old villain is making a comeback — but with its reputation newly burnished.

Banned from pharmacy shelves worldwide in the 1960s because it was causing birth defects, thalidomide seems to hold exciting new promise as a weapon against TB, says **Gilla Kaplan**, PhD, associate professor at the laboratory of cellular physiology and immunology at the university.

Thalidomide, used as a sedative decades ago, is now being studied for potential beneficial effects on diseases as diverse as AIDS, breast cancer, and multiple myeloma. In the field of TB research, work on immune system modulation is among the most exciting. Within that sphere, Kaplan's work has been pegged as edge-of-the-seat stuff. "She's definitely the one to watch," says **Clifton Barry III**, chief of the mycobacterial research unit at the National Institute for Allergy and Infectious Diseases in Bethesda, MD.

Drug could boost immunity against TB

One of thalidomide's many puzzles is its ability to hide one effect inside another, like nested boxes. To begin with, the drug exerts certain effects on the cytokine known as tumor necrosis factor alpha, or TNF-A. That cytokine is thought to be responsible for most of the pathology associated with TB: the wasting, tissue damage, night sweats, fevers, and weakness. Thalidomide appears to reduce the soluble molecules associated with those symptoms, Kaplan says.

Thalidomide doesn't reduce cytokine too much, which is a good thing Kaplan adds. "Without TNF-A, we don't get the recruitment of white blood cells to the site of infection, or the walling off the infection. With insufficient TNF-A, we'd get disseminated, or miliary, TB. So it's a fine balance."

Thalidomide also appears to boost the immune system by acting as a co-stimulatory molecule to increase the level of activation of T-cells, which play an important role in immunity against TB, says Kaplan. That may be the reason TB infection never becomes active in some people.

It's too soon to tell for sure, but thalidomide

may have two important roles in the fight against TB. "First, it may help protect the body against infection," she says. "Second, it may attenuate the immune response that drives the pathology."

Kaplan's work could provide a much-needed key to unlock the intricacies of how TNF-A works in humans. In animal models, its role is fairly well-understood, she explains, but in people, that relationship needs further elucidation. "So part of what we're doing is seeking proof of concept as a way to understand and analyze the pathology of TB. And another part is to see if we can intervene in a way to improve outcome."

Her work in small trials involving humans already has begun to show that using thalidomide to improve therapy's outcome may indeed be possible. In pilot studies with patients co-infected with HIV and TB, Kaplan has shown that thalidomide stimulates T-cells. The next challenge is to prove that a beneficial effect is likewise produced in patients contending only with TB.

The relationship between the drug's ability to cause birth defects and its promise as an ally in the fight against TB is another puzzle, Kaplan adds. "We don't know how thalidomide causes birth defects — whether it has to do with the same properties that impact the immune system or with different ones, and whether its ability to cross the placenta is key to the damage it does or not."

With researchers striving to find analogs of thalidomide that don't cause birth defects, some of those questions soon may be answered as well. ■

Rifampin acceptable in some TB/HIV instances

Skeptical clinicians say rifabutin is fine, thanks

When rifampin recently was restored to the armamentarium of clinicians treating TB patients on protease inhibitors for their HIV, the occasion didn't exactly excite the world of HIV therapy.[1] It did, however, serve to remind everyone of just how complicated the jobs of infectious disease specialists have become.

In the past, rifampin, a pillar of TB treatment today, had not been recommended in instances in which patients were concurrently taking other drugs — in particular, protease inhibitors — that interact with it. Physicians contacted about the government update giving them permission to use rifampin, at least in certain situations, say they're not planning to make any sudden moves, new guidelines or not.

"With all the new antiviral agents, things have gotten really complicated," says **Elena Hollender**, MD, director of clinical services at the A.G. Holley Hospital in Lantana, FL. "We spend most of our time walking on tiptoes as it is already. I think in this case, most of us would say, 'Tread cautiously.'"

The update, published in the Centers for Disease Control and Prevention's March 10 *Morbidity and Mortality Weekly Report*, tells clinicians they now can use rifampin in the following three situations:

- in patients whose antiretroviral regimen includes efavirenz, a non-nucleoside reverse transcriptase inhibitor, and two nucleoside reverse transcriptase inhibitors (NRTIs);
- in patients whose antiretroviral regimes include the protease inhibitor ritonavir and one or more NRTIs;
- in patients whose antiretroviral regimen includes the combination of the two protease inhibitors ritonavir and saquinavir in either the hard-gel or soft-gel formulation.

The update also strongly recommends the following:

- reducing the dose of rifabutin to 150 mg two or three times per week when it's given to patients taking ritonavir, with or without saquinovir in either the hard or soft formulation;
- increasing the dose of rifabutin to either 450 mg or 600 mg daily, or 600 mg two or three times a week, when rifabutin is used concurrently with efavirenz.

Although it's always good to have another option, Hollender says she's grown comfortable working with rifabutin and plans to stick with it. "It's nice to have another choice," she says. "And there may well be a place for rifampin in certain situations. But personally, I would like to see more data about dosage adjustments."

True, rifabutin costs about $4 more per dose than rifampin, but conventional wisdom dictates that not having to worry about side effects more than makes up for the extra cost. Arguments for trying rifampin probably would be more compelling if rifabutin were causing problems, but it isn't, says Hollender. "There's no problem with tolerability, and from what we know about the mechanism of the drug, it should have about the same efficacy."

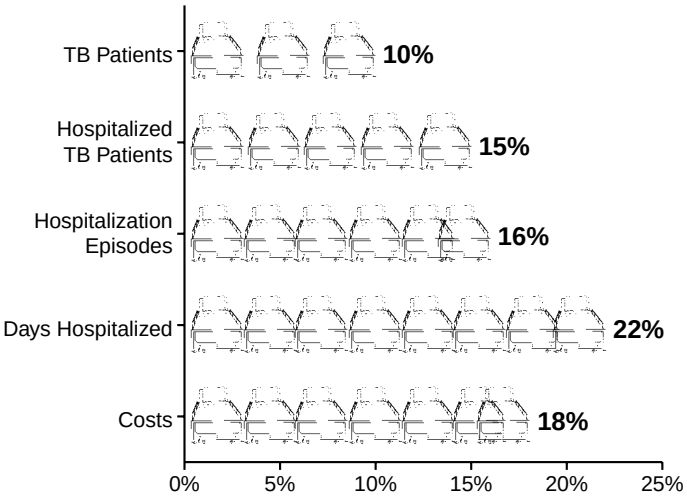
Rick O'Brien, MD, chief of the Research and Evaluation Branch of the Centers for Disease

Control and Prevention's Division of TB Elimination, agrees. "I don't treat HIV patients in my practice, but I can tell you that rifabutin is a good drug," he says. "It's generally well-tolerated; in fact, it may be a bit better tolerated than rifampin. Plus, we've got good data on its efficacy. It's actually got a slightly longer half-life than rifampin."

Anyone who wants to give rifampin a try in one of the new combinations listed in the update, Hollender says, should monitor blood levels of the drugs as a safety net. "We already have patients on whom we do this, both for their TB drugs and their protease inhibitors. With the advent of people perhaps turning to ritonavir or saquinovir, there may be another role for drug monitoring."

Reference

1. Centers for Disease Control and Prevention. Notice to readers: Updates guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2000; 49:185-189. ■



Of 1,493 TB patients surveyed, 10% were homeless, but that 10% incurred nearly 20% of the total reported costs. They also incurred more than their share of hospitalization episodes and hospitalization days. *Source:* Copyright 2000 by the American Public Health Association, Washington, DC.

Hospitalization increases costs of treating homeless

Housing, early care could reduce price tag

Homeless TB patients without insurance and homeless TB patients with HIV infection run up bigger hospital bills than other TB patients — on average, about $2,000 more, a recent study found.[1]

To help trim those costs, programs should provide free housing and early access to medical care, according to **Suzanne Marks**, MPH, medical epidemiologist with the Division of TB Elimination (DTBE) at the Centers for Disease Control and Prevention in Atlanta and lead author of the study.

The higher price tag reflects two aspects of hospitalization costs that Marks looked at: frequency and duration of stay. In general, HIV-infected homeless TB patients tended to have more frequent hospital stays than their housed counterparts. Providing early access to available health care could help homeless HIV-infected persons get testing and counseling and may help them avoid progressing from TB infection to full-blown disease, says Marks.

As for uninsured homeless TB patients, providing alternative housing could be expected to help them avoid long stays, assuming they're in the hospital at least in part for lack of a better place to go.

Many TB control programs are notable for strides they've made in providing housing. San Francisco, Seattle, New York City, San Diego, Los Angeles, and Phoenix all boast strong alternative housing programs, says **John Seggerson**, associate director for external relations at the DTBE. "We encourage other programs to establish working relationships with their local and state housing authorities, too," he adds.

Housing program saves money

For HIV-infected TB patients, Marks adds, there's an important federal housing program known as Housing Opportunities for Patients with AIDS (HOPWA). "It's hard to overestimate the value of programs like HOPWA," she notes.

Taxpayers generally get stuck paying for the extra $2,000 in hospital costs homeless TB patients incur, at least in instances where patient costs aren't covered by Medicaid or by benefits available to veterans, she says. At about $35 a day for food, meals, and directly observed therapy,

providing alternative housing is a bargain, since hospital rooms run up to 20 times that much, Marks says.

Severity of illness wasn't evaluated in her study, she notes, so it's hard to know how many homeless TB patients would benefit from the interventions she proposes and how many would wind up in the hospital regardless.

Reference

1. Marks SM, Taylor Z, Burrows NR, et al. Hospitalization of homeless persons with TB in the United States. *Am J Publ Health* 2000; 90:435-438. ■

UV shelter study: Sunny with few conversions

Or, decorating quirky spaces with killer lights

Preliminary data are coming in from a six-city study of ultraviolet (UV) germicidal radiation in homeless shelters. If anything, the results suggest that from the researchers' pont of view, something's working a bit too well.

Counting sites with both real and placebo lights, there have been only two skin-test conversions recorded so far, making it tough to measure differences between intervention and control settings.[1] Researchers say that far from being disccouraged, they're heartened by the early results.

"Certainly, the national effort to implement directly observed therapy has had a marvelously beneficial effect on TB control," says **Philip Brickner**, MD, chairman of the department of community medicine at St. Vincent's Hospital in New York City and lead researcher in the study.

"But when I talk to my colleagues who are working with the statistical part of the study," he says, "they say not to worry [about the paucity of conversions]. If we're out there with our 'net,' sooner or later we'll catch some converters."

Shelters in six cities across the country will serve as their own basis for comparison, with placebo UV lights operating in a double-blind setup for part of the time.

The aim of the study is to find out once and for all whether UV lighting is truly the inexpensive deterrent to disease transmission its boosters believe it to be. To answer that question, Brickner and colleagues are studying high-incidence areas. "We're working in cities where TB rates are far higher than average," he says. "As a separate demographic group, their rates are consistently running 10, 20, even 30 times higher than those of the general population."

As soon as researchers receive necessary funding, sites will begin operating in shelters in Los Angeles, where, with the city's high incidence of TB infection among the foreign-born, rates of conversion should be higher than they've been so far.

The sites already producing data are in Birmingham, AL, New Orleans, and New York City. Additional sites in Houston and in four smaller towns in south Texas should be coming on board soon, Brickner adds.

If UV light works, "it will be the cheapest way by far we'll have of preventing disease."

In the meantime, researchers have been refining the art of installing UV fixtures in the most difficult spots imaginable, he says. Besides their occupants' higher-than-average TB rates, shelters were selected precisely because of their architectural quirks. If UV light could work under such trying conditions, researchers reasoned, it could work anywhere. "The shelters [where we're working so far] represent an enormous diversity of spaces," he says. "And even so, they've all been functionally fitted out. I'm no engineer, but I've been able to learn what goes into the decision about where to place fixtures."

Project engineers have come up with plenty of creative solutions, he adds: For example, when ceilings are extremely low, they hang a box containing a UV light and a fan on the wall. Nor has safety presented a problem: None of the fixtures has resulted in painful eye irritations or skin burns associated with improper UV light exposure.

Brickner emphasizes that he's neutral on the subject of whether UV light ultimately will prove effective against TB. "But if it does," he adds, in comparison to administrative or ventilation solutions, "it will be the cheapest way by far we'll have of preventing disease."

Reference

1. Brickner PW, Vincent RL, Nardell EA, et al. Ultraviolet upper room air disinfection for tuberculosis control: An epidemiological trial. *J Healthcare Safety, Compliance, Infect Control* 2000; 4. ■

Putting a dollar sign on TB in Amsterdam

One TB/HIV case = school costs for 10 kids

Ministers of health and finance from 20 of the 22 "high-burden" countries have signed a declaration in which they promise to try harder to fight TB but also warn they'll need more help from rich countries if they're to succeed.

As that part of the declaration reads: "While it is first and foremost the responsibility of affected countries to take the necessary actions . . . against tuberculosis, the problem is often the greatest in the very countries which can least afford to take action."

Rich countries that think TB isn't their problem may be in for a surprise, said U.S. Secretary of Health and Human Services **Donna Shalala** at the March conference in Amsterdam where the ministers of health and finance met for four days. Shalala cited findings from the new World Health Organization report on global drug resistance that show resistance rates up by 50% in three developed countries. "There's no way to build a 'fortress America' or a 'fortress Europe' against TB," she added.

Before heading home, the ministers also promised to expand coverage of WHO's approved strategy known as directly observed therapy, short-course (DOTS) by ensuring 70% case detection by the year 2005. In addition, they affirmed WHO's proposal to create the Global Fund for Tuberculosis.

Good intentions notwithstanding, new drugs are urgently needed, said **Jim Orbinsky**, head of Doctors Without Borders. Orbinsky leveled blasts at the drug industry for its focus on "finding another cure for impotence or baldness. Governments either need to regulate the industry more closely or "establish their own capacity to promote research," he added.

No matter what the outcome, the fact that the conference took place at all was cause for celebration. "It was extremely exciting to see so many ministers of health gathered to talk about just one disease. That's never happened before," says **Bess Miller**, MD, associate director for science at the Division for TB Elimination at the Centers for Disease Control and Prevention in Atlanta.

For some ministers, the high energy continued after the conference disbanded. The South African Minister of Health, for one, e-mailed Miller excitedly about the noisy press conference she found waiting for her when her plane touched down at the airport.

When they weren't talking about the need for better access to affordable drugs or the troubles that afflict countries that use DOTS but are bedeviled by high rates of HIV or multidrug-resistant TB, the ministers listened to speakers hammer home the conference's stated theme of how TB hurts economic growth.

"Health expenditures to fight TB and HIV epidemics will force very hard trade-offs in public finance if we don't act now," explained **Mieko Nishimizu**, the World Bank's president of the South Asian region. Nishimizu and **Gro Bruntland**, MD, director general of WHO, drew examples from India to portray the enormous financial dimensions of the problem.

TB costs India $2 billion a year

Each year, Bruntland said, more than 300,000 Indian school children must abandon their studies because a parent falls ill with TB, and each year, more than 100,000 Indian women are evicted from their homes because of the social stigma of the disease. The average cost of treating one TB patient co-infected with HIV exceeds that of educating 10 children in primary school, Nishimizu added. In sum, TB's net cost to the Indian economy is $2 billion a year, Bruntland said.

Poor countries that put off dealing with TB now will pay dearly later, the two added. "Literally, this is a public health crisis where $10 worth of prevention is worth $5,000 of cure," said Bruntland. "If we are careless in providing that $10 treatment the first time, the next time treatment will cost $5,000 or more." ■

Clinton gives child DOT

During his recent trip to India, President Clinton observed World TB Day by giving a 12-year-old TB patient her last dose of medication. Then Clinton signed the register documenting that the child had completed her cure. "The spread of disease is the one global problem from which no nation is immune," he said afterward. ■

Resistant TB on the rise in Western countries

Denmark, Germany, New Zealand see increases

TB controllers in some Western countries who thought they might be spared the rising global tide of TB resistance are beginning to feel the water lapping at their toes, suggests a new report on global TB resistance from the World Health Organization.

"Findings from Western countries show that multidrug-resistant TB [MDR-TB] has established, if not a beachhead, at least what I'd call a toehold," says **Nils Daulaire**, MD, president of the Global Health Council, an advocacy group based in New York City. "It also shows that MDR-TB has established a solid hold in lots of countries around the world: in Iran, surprisingly, and also in Estonia, Latvia, India, China, and Russia."

Findings show "that MDR-TB has established a solid hold in lots of countries around the world."

In Denmark, the proportion of cases resistant to at least one drug rose from 8.8% in 1996 to 13.4% in 1997; in Germany, from 7.7% in 1997 to 10.3% in 1998; and in New Zealand, from 4.8% in 1996 to 12% in 1997.

Drug resistance should be considered threat

The proportion of MDR-TB cases in those countries is lower, at less than 2%. Foreign-born patients in the three countries are twice as likely as native-born patients to be harboring a drug-resistant strain. In the United States, the report says, resistance to at least one drug is down slightly, from 12.9% in 1995 to 12.4% in 1997.

During that same period, MDR-TB in the United States fell from 2% to 1.4%, but in Mexico, America's neighbor to the South, 20.6% of cases show resistance to at least one drug; and 6% of new and previously treated cases represent multidrug-resistant TB.

The time when critics could say TB advocates are "over-promoting the issue" of drug-resistance has come and gone, adds Daulaire. "It's now clear that MDR-TB has become an important and growing concern."

CE objectives

After reading each issue of *TB Monitor,* health care professionals will be able to:

- Identify clinical, ethical, legal, and social issues related to the care of TB patients.
- Summarize new information about TB prevention, control, and treatment.
- Explain developments in the regulatory arena and how they apply to TB control measures.
- Share acquired knowledge of new clinical and technological developments and advances with staff. ■

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Daulaire praises the WHO report for its ability to show how swiftly resistance rates are rising in hot spots around the world. In Estonia, at the top of the list, the percentage of MDR-TB stood at a whopping 18.1% in 1998, up from 13.5% in 1997.

MDR-TB also accounts for more than 3% of all new cases in the following areas:

- two provinces in China;
- India;
- Iran;
- Mozambique;
- an oblast in Russia.

In Mexico, Italy, and Israel, MDR-TB is found in more than 6% of both new and previously treated cases.

By the yardstick of resistance to at least one drug, the report shows 13 areas in which total caseloads reflect resistance rates of 20% or more **(listed in box)**:

- ✔ Estonia, with resistance levels to one or more drugs stand at 40.8%
- ✔ China's Henan province, with levels at 40.5%
- ✔ Russia's Ivanovo oblast, at 39.5%
- ✔ Latvia, 30.1%
- ✔ Sierra Leone, 27.7%
- ✔ China's Shandong province, 24.5%
- ✔ India's Tamil Nadu state, 24.1%
- ✔ Mozambique, 23.1%
- ✔ Uganda, 22.1%
- ✔ China's Zhejiang province, 21.9%
- ✔ Mexico, 20.6%
- ✔ Italy, 20.5%
- ✔ Russia's Tomsk oblast, 39.3%

Countries in which DOTS has been employed rigorously are finding that resistance rates are leveling off or even starting to go down. In parts of China where DOTS has been implemented, resistance rates are three times lower than in non-DOTS regions, and in Cuba and Nepal, resistance rates are heading downward as well.

There are exceptions to that rule, however. In Botswana and Tanzania, good DOTS programs show evidence of being overwhelmed by HIV. ■