

TB MONITOR™

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TB controllers scalded as HIV prison debate begins to boil over

TB docs ponder coercing inmates to take INH

In recent months, jails and prisons that don't have all the elements of TB control tightly in place have been finding themselves caught uncomfortably in the spotlight. In most cases, it's not even TB outbreaks that trigger the initial scrutiny.

What seems to be going on instead is that as the debate over health care for HIV-infected inmates heats up, those charged with controlling TB are getting caught in the backslash.

In Atlanta, for example, two overcrowded jails that serve adjoining counties are both under court orders to clean up their TB control acts. What launched the first of two class action lawsuits (filed by the Atlanta-based Southern Center for Human Rights) were complaints about medical care being withheld from HIV-infected inmates in Fulton County jail. Fulton County includes much of Atlanta. That lawsuit eventually expanded to address shortcomings in TB care as well.

In the second investigation, TB care at neighboring Dekalb County jail has come under considerably heavier fire, with the judge presiding over the case ordering a long list of TB-related improvements.

County TB controllers complain off the record that they've been desperately short-handed, and that the jail's private health care subcontractor hasn't wanted any TB-related advice. They also seem to have developed terrible cases of phone-call phobia.

"I'm familiar with lots of jails around the country, and what surprised me here in Atlanta was the absolute paucity of attention to all matters of public health - including HIV, TB, and sexually transmitted diseases," says **Robert Griefinger, MD**, court-appointed monitor for the two cases, and chief of the New York City-based Bromeen Group.

Griefinger's comments underscore the subtext of both investigations: the growing national debate over

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Time will tell — literally

A new compliance monitor for TB patients is designed to look and act like a standard Casio wristwatch, only this one will beep when it's time for patients to take their TB meds, and even thank them when they do. It also will snitch on those who don't take their meds 126

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Risk said lower for health care workers

Research presented recently during a workshop at the Institute of Medicine (IOM) on regulating occupational exposure to TB suggests that health care workers are at a much lower risk for developing TB than experts had thought. Workshop participants addressed the adequacy of current government guidelines for protecting health care workers against TB infection, looking at the potential for stricter measures from the Occupational Safety and Health Administration 128

The debate over Aplisol and Tubersol

False-positive reactions to a tuberculosis skin-testing reagent are causing a stir among hospital employees and officials. One month after switching from Aplisol to Tubersol, 11 health care workers in Atlanta had a skin-test conversion, but chest radiographs showed no evidence of tuberculosis, and retesting with the Tubersol purified protein derivative came out negative. This caused one infectious disease authority to challenge a recently published study concluding that Aplisol and Tubersol are equivalent. 128

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how much health care jails and prisons owe their inmates.

The premise that inmates of correctional facilities are at increased risk for infectious diseases of all sorts isn't news. In the wake of court rulings that mandated increased screenings, Atlanta's Fulton County jail began doing syphilis testing; fully 7% of the jail's inmates were found to be positive.

Prevalence of other infectious diseases in jails and prisons is equally breathtaking. Nationwide, for example, about 25% of HIV-positive people pass through jails and prisons, as do 30% of the country's hepatitis C cases, says **Anne De Groot, MD**, co-chair of the HIV Education prison project at Brown University School of Medicine in Providence, RI.

Getting attention with drug-resistant HIV

What is new is how human-rights advocates such as De Groot and the Southern Center for Human Rights have begun using the specter of the spread of infectious disease — especially drug-resistant HIV — to force correctional systems' hands. "There's every reason to expect that the spread of HIV-resistant strains will become more commonplace, given the concentration of HIV-infected individuals in settings where HIV care is substandard," De Groot says. She adds that the current situation "closely resembles" the point at which multidrug-resistant TB began to spread beyond the correctional setting in New York State.

In TB control circles, the debate over jailhouse health care has taken an interesting twist of its own. Because so many inmates in correctional settings are TB-infected, the argument goes, why not work harder at getting preventive treatment into them?

Indeed, the Institute of Medicine's report on TB elimination released last year breaks with tradition and recommends a new, strong-armed approach to jailhouse prophylaxis, suggesting that prisons begin using measures such as a "tuberculin hold" status to lock down inmates who refuse preventive medicine. (See: **Institute of Medicine. *Ending Neglect: The Elimination of Tuberculosis in the United States*. Washington, DC: National Academy Press; p. 101.**)

For the last four years, that's exactly what New York State prisons have been doing, says **Lester Wright, MD, MPH**, chief medical officer for the state's prisons. So far, courts that have heard

cases related to the policy have ruled in favor of the state prison system.

Is this a good thing? Several experts interviewed by *TB Monitor* answered with an emphatic “no.”

“The idea of forcing people to take prophylaxis for TB infection is based on ignorance,” says **Ronald Shansky**, MD, a Chicago-based correctional health care consultant and a board member of the Chicago-based National Commission on Correctional Healthcare (NCCH). “The overwhelming majority of inmates identified as having TB infection will take the medicine voluntarily if you give them proper counseling.” Besides, he adds, in most places, TB control in jails and prisons is working well; falling TB rates in the community reflect that fact. “So why,” he asks, “do we need to add compulsion?”

Edward Harrison, president of NCCH, agrees. “Coercive practices can result in an adversarial relationship between inmates and health care providers, and that’s not something you want,” he warns. “What’s much better is to develop a relationship of trust. Inmates in some places are used to having stuff shoved down their throats, but that can be very bad for patients. It’s also bad for the community once the patient gets released.”

Wright says he worried about that when he first came up with the idea of tuberculin hold, which is based on the premise that an inmate is most likely to come down with TB in the first year after infection and that infected inmates have been recently infected. “So far it hasn’t been a problem, though,” he says.

Plus, Wright adds, most inmates don’t need a lot of coercing — just a good explanation of the risks and benefits. “Most people understand and accept that taking [treatment for latent TB infection] is for their own good, and for the good of the community,” he says.

Moreover, Wright believes the opportunity to give such treatment in the prison setting is simply too good to pass up. “The correctional setting is truly an excellent place to do public health,” he says. From TB control’s new emphasis on identifying and treating infection, it follows that jails and prisons have a mandate to do what they can. Where else in America, he asks, can someone be supervised so easily through an entire course of preventive therapy?

“Here, it’s manageable,” he concludes.

“Anywhere else, people get tired of it, and they quit before they’re finished. If this country really wants to focus on latent infection, correctional settings are the logical place to do it.” ■

Making DOT state law helps Colorado hold line

When caseloads heat up, statute serves as firewall

Directly observed therapy (DOT) has been the law of the land in Colorado since 1998. In the two years since the statute was quietly placed on the books — with scarcely any fanfare, according to TB experts in the state — it’s had surprisingly little impact on private-sector practices. That’s because even though about half of the TB cases in the state are managed by private providers, community physicians were already in the habit of referring patients to public-health clinics for the DOT part of their treatment by the time the law was passed, says **Ellen Mangione**, MD, MPH, director of the state’s division of infectious diseases.

What the statute has done is help hold the line in the public health sector, Mangione says. “Sometimes our public health nurses get to feeling a bit overwhelmed, and that’s when this statute helps to hold them to the [DOT] standard. You could say it’s been helping us to maintain.”

At the same time, state TB experts agree the statute has probably helped strengthen existing links between the private and public sectors.

“With this statute, we’re not trying to tell private providers they can’t treat their own patients,” says **Richard Hoffman**, MD, medical adviser to the state TB control program. “We just wanted to send the message that if you couldn’t provide DOT yourself, you could turn to the public sector to provide it, or else you’d have to get an exemption.” Hoffman has granted just one exemption, for extra-pulmonary TB, since the regulation went into effect.

Law meant to strengthen private/public links

Mangione agrees that the relationship between the private and public sectors here is a congenial one. “We see TB care as very much a partnership,” she says. “We try very hard to hook folks up to a private physician in their community and keep them hooked up. The private physicians are the ones who provide follow-up, and they’re also able to give a level of care you just can’t expect from the public sector.”

Once a private physician takes on management of a TB case, the public sector, along with provid-

ing DOT, functions mostly as a support system, she adds. “We fill the prescriptions for the medications. We make sure the patient comes in for repeat chest X-rays. And we assist with referrals if the patient gets into trouble. It’s really a division of labor.”

In Alabama, where DOT is the standard of care (as it is in Mississippi and South Carolina), TB experts say they’d love to have a law like the one in Colorado. “Even though we start 98% of our cases on DOT, there are still some private physicians around who don’t think it’s really necessary,” says **Nancy Brook**, MPH, the state’s TB program manager. “It would be really interesting to see what impact such a law would have on the medical community here.”

According to Mangione’s records, rates of DOT in Colorado continued a steady climb once the 1998 statute was passed, evidently without much help from the new law. In 1993, DOT rates stood at 53% of all patients with pulmonary TB; by 1996, that rate was up to 74%; and by 1998, 93%.

As African-born cases rise, programs adjust

Earlier age, quicker onset among this group’s trends

In Seattle, this year’s TB case totals will reflect a shift in demographics that has left public health experts here slightly amazed. For the first time, foreign-born TB cases from Eastern Africa will outnumber those from Southeast Asia.

“That’s something I never thought I’d live to see,” says **Charles Nolan**, MD, chief medical advisor to the TB control program in King County, which includes Seattle.

Most of the African cases are turning up among refugees fleeing war, famine, and unrest in Somalia, Eritrea, and Ethiopia in the Horn of Africa.

To a lesser extent, the increase in African-born cases is reflected in what’s going on at the national level. Nationally, this year’s ceiling for African refugees is 18,000, up from last year’s ceiling of 13,000, according to U.S. State Department figures. As in Seattle, the majority of the 85,000 African refugees who’ve been admitted to the U.S. since 1980 are from Ethiopia (which has supplied over 30,000 refugees) and Somalia (around 25,000), with smaller numbers of Sudanese, Liberians, Zairians, Rwandans,

Here’s where the statute has really helped. Even though case totals have held fairly steady, the complexity of some cases has increased as more cases involving drug-resistant strains have begun to appear, says Mangione. That means overworked public-health nurses may be occasionally tempted to slack off on DOT.

“In 1998, 18% of our cases involved resistance,” mostly among foreign-born residents from Eastern Europe, she says. “Those cases are often more complicated and more time-consuming.”

In addition, an increasing number of foreign-born cases arrive with no private insurance, which means the public health sector can’t subcontract out DOT duties (to a visiting nurses’ association or the like) when things get especially busy.

Under ordinary circumstances, public health nurses might be forgiven for letting some patients just come in once a month and pick up their pills. With the statute to back them up, says Mangione, “We tell them, ‘Sorry, you can’t do that — it’s the law.’” ■

Ugandans, and Angolans rounding out the pie. The pool of African refugees is also growing increasingly diverse, with citizens from 43 African nations admitted to the U.S. last year.

In Seattle, the shift in demographics has dictated a shift in TB control program strategies, because the East African cases differ in several ways from other foreign-born groups the area had grown accustomed to seeing, Nolan says. “First, we’re finding that active disease onsets earlier after arrival and in a younger age group. We’re also seeing more extrapulmonary disease, including a good bit of Potts Disease [TB of the spine],” says Nolan.

Cases among the young and in extrapulmonary sites present in a variety of ways and thus can be tougher to spot, he adds. “We’re trying to alert the medical community to this fact and get them to think about it more.”

As for earlier onset, experts in Seattle have determined that about 30% of the active cases among east Africans occur within the first year after arrival in the United States, and 80% of cases occur within the first five years. By comparison, about half of the cases among other foreign-born groups occur within the first five years.

“That means outreach to these groups is really important,” Nolan says. “We’ve got to get them as soon as we can, screen them, and, assuming they’re infected but free of active disease, get them on treatment for latent TB infection. That’s

another message we're trying hard to get out to primary health care providers."

What's new in Seattle sounds like a rerun to TB controllers in Minnesota. There, the biggest group of caseloads tipped from Asians to East Africans in 1996, says **Deb Sodt**, RN, head of the state TB program. Somalis make up the biggest group of all TB cases, followed by American-born patients and then by Ethiopians, Sodt says. Asians don't make the list until the number-four spot, which is occupied by Vietnamese people.

Many of the same trends Seattle TB experts are spotting also hold true in Minnesota, says Sodt. The Minneapolis area, especially, is a favored site for secondary migration, as refugees relocate there from other parts of the country hoping to land a job in the booming economic climate. "We're definitely seeing early onset of disease, with our biggest group in their 20's, followed by [patients in their] early teens," she says. As in Seattle, clinicians here are also seeing more extrapulmonary cases, particularly lymphatic TB, Sodt says. "Usually it's present in just one or two nodes," she says. "It also tends to go with earlier presentation." ■

These 'pork barrels' hold global MDR-TB projects

Post reporter, Sen. McCain should check facts

An editorial writer at the *Washington Post* purported to alert readers across the nation to a wasteful ripoff of taxpayer money intended to help TB victims abroad. It was described as a pork-barrel project intended to siphon big bucks from a foreign-aid spending bill and deposit the money into a little-known institute in Alabama.

The only trouble is that the "little-known institute" — the Gorgas Memorial Institute — has a world-class reputation for training clinicians in tropical medicine. As for the recipients of the USAID money, they're not (as *Post* editorialist Sebastian Mallaby implied) close relatives to Rep. Sonny Callahan, the Alabama congressman who had a hand in drafting the foreign-aid bill.

Instead, the two men painted as villains turn out to be **Richard Chaisson**, MD, assistant professor of medicine at Johns Hopkins University Medical School and chief of the Baltimore TB clinic, and **Michael Kimerling**, MD, MPH, a consultant to

Medecins Sans Frontieres and assistant professor of medicine and public health at the University of Alabama School of Medicine in Birmingham (UAB).

The editorial ruffled a few feathers and has also provided Kimerling and Chaisson's colleagues, who are more than aware of the duo's contributions, with a few chuckles. "To tell you the truth, I haven't noticed any drastic changes — no fast cars or luxury cruises — in Michael's behavior lately," laughs **Nancy Dunlap**, MD, PhD, medical director of the Alabama state TB program.

Kimerling says he spotted the editorial (which drew heavily from Sen. John McCain's web site compendium of pork-barrel projects) on a recent flight home from Russia, where he was working on the epidemic of multidrug-resistant TB threatening to overtake Russia's overcrowded prison system. He thought briefly about writing a letter to set Mallaby straight, he admits, but has been too busy with work to do so.

Chaisson, for his part, says he can't even muster much indignation. "It's too bad they wrote it, but I don't think debating them in print will help any," he says, in a voice that sounds as if it's usually reserved for students who fall asleep in anatomy class.

As for the Gorgas Memorial Institute, a busy political reporter might be forgiven for not having heard of it. Established at the turn of the century, it originally functioned as a prestigious school of tropical medicine situated in the Panama Canal. It was created by Congress with an eye to serving the needs of American military forces stationed in the tropics. After the Canal Zone was returned to Panama, Gorgas was downsized and relocated to the University of Alabama at Birmingham, where it still runs a modest but highly regarded program to train students in tropical medicine.

Once they had determined to collaborate on a number of international TB and HIV projects, Chaisson and Kimerling say they decided to use Gorgas as an intermediary in the partnership between the two medical schools.

In case you were wondering, here's a sampling of what Kimerling and Chaisson are doing around the world with their share of the USAID-authorized TB funds:

- **The state of Veracruz in Mexico:** Chaisson and Hopkins colleagues will provide technical support and collect data for a project that will establish a model program for identifying and treating MDR-TB in Mexico.

- **A slum in Lima, Peru:** Working in a setting that has some of the highest rates of morbidity and mortality for HIV/MDR-TB on earth, the Hopkins group will use novel, costly techniques to make super-rapid TB diagnoses.

- **Brazil:** In a rural inland area near Rio de Janeiro, the Hopkins group will collaborate with what they hope will serve as the nation's model program for directly observed therapy, short-course (DOTS). The program, which has already moved treatment success rates from 60% to 84% in its first year of existence, is especially important, Chaisson explains, because Brazilian TB experts so far have resisted the introduction of DOTS programs. "It's sort of like in Russia, where the attitude is, 'We're not a third-world country, so stop trying to sell us on this third-world approach to TB control,'" Chaisson explains.

- **Russia:** Kimerling is a regular commuter there, visiting grim prisons where he is trying to work the kinks out of one of the world's first models of the World Health Organization's new

DOTS-Plus strategy. This is an attempt to develop sustainable therapeutic models for containing and controlling MDR-TB in parts of the world where MDR has already spun beyond the control of regular DOTS programs.

- **Cambodia:** Kimerling and the UAB team will conduct HIV prevalence surveys and will work to integrate and provide cross-training to the country's HIV and TB programs, partly by adding a TB component to a program that provides home care to about 700 symptomatic HIV patients in the Phnom Penh area and which is about to expand coverage substantially.

- **Indonesia:** The UAB team will establish DOTS programs in hospitals, linking them to the national TB program, Kimerling says. "Again, our goal there is to strengthen the national TB program and try to get hospitals to follow the DOTS strategy," he adds.

He pauses for a beat. "And hey, if that's pork-barrel . . . well, maybe we should be doing more of it." ■

Hey, pal, got the time? Time to take your meds

New compliance monitor from Sequella

Someday soon your wristwatch might be able to tell you a lot more than whether you're late to work.

A new compliance monitor for TB patients is designed to look and act like a standard Casio wristwatch, says **Leo Einck**, PhD, chief executive officer of Sequella, Inc., the for-profit half of the Rockville, MD-based foundation by the same name that "incubates" promising new TB research.

Unlike a Casio, though, Einck's wristwatch will beep when it's time to take your TB meds; then, once it sees you've done so, it politely says, "Thank you." Non-compliers (or folks who forget to put their watch back on after they take a shower) will hear another beep. Both kinds of events will be recorded on a computer chip in the watch, waiting to be downloaded and read by a health care provider.

The gadget works not by recording the removal of a pill from a blister-pack (or some other such activity), but by "seeing" the pulse of a fluorescent tracer chemical released into a patient's bloodstream after he or she swallows the pill. That's why this one (unlike other a long

string of other compliance-monitoring gizmos that have crashed and burned) can't be foiled or fooled, Einck asserts.

Plus, the watch really does keep time and will look and cost about the same as a inexpensive wristwatch, with a Swatch-like assortment of wristbands for extra appeal. The difference is that along with the usual works, the Sequella time-piece will contain "quite an elegant optical filtering system, which essentially makes the skin invisible," Einck says.

Boxful could get DOTS program up and running

Positioned over the volar, or underside, part of the forearm (where the veins run close to the surface), the optical device will "see" a pulse of flourescine, a harmless agent added to the drug "just like cornstarch, or any other excipient," Einck says. The optical device monitors only the flourescine, not the drug itself; but since the flourescine will be mixed into the pill contents, there's no way to trip the recording device except by taking the pill, Einck adds.

Flourescine is already used in retinal scans, he points out, and the amount that will be added to the TB drugs is so minute that it would take "years and years" to equal the amount used in a single scan.

So far, the system has been tested only in the lab, where it's worked well in animal tissue.

Sequella has secured a grant to fund the next two steps: construction of a prototype device and safety tests in humans.

Obviously, such a device, if it works, can be used to monitor compliance in many fields other than just TB, Einck says. But TB programs, habitually weighed down by the extra burdens of supervising six months of therapy (which could only be termed “short-course” in the long-suffering world of TB control), might welcome such a device even more heartily than fields such as diabetes or epilepsy, two other places Einck also sees as potential markets.

“In TB control, we’ve never really had a system for monitoring compliance that relies on anything other than some kind of enforcement, either a nurse who watches you take the pills or a judge who puts you in jail for not taking the pills,” says Einck. “This way, you really have an opportunity to take a boxful of these watches and use them run an effective DOTS program.

In areas where there simply isn’t enough money to do it the old-fashioned way — poor countries, for example, where more pressing problems have kept expensive TB control programs pushed to one side — “you could really get the ball rolling with these things,” Einck adds. ■

Post-treatment INH works, but it’s hard to say why

Loss of isolates precludes RFLP testing

HIV-positive TB patients who have finished treatment and show signs of immunocompromise should be considered for post-treatment TB prophylaxis, says **Warren Johnson**, MD, the B.H. Kean professor of tropical medicine and chief of the division of international medicine at Cornell University.

In a country like Haiti, where TB is endemic, such patients should be certainly considered for lifelong post-treatment prophylaxis — perhaps even lifelong prophylaxis, he adds. In Haiti, Warren and other researchers found that giving 12 months of isoniazid to such patients dropped the incidence of recurring TB in HIV-infected patients significantly, from 7.8 per 100 person-years to 1.4 per 100 person-years.

The trouble is that Johnson (whose research was published recently in *The Lancet*) doesn’t know whether the recurrences reflected relapses of old disease or a new infection, because some of the strains that were to be tested were lost. “So we don’t have RFLP [restriction-fragment-length polymorphism] or other markers to indicate whether the recurring TB was exogenous or endogenous,” he says. “I wish we had the information.”

From a practical standpoint, it didn’t make any difference to the group in Haiti, he points out. “They had TB, so they had a problem,” he says. For patients in other areas where TB is endemic and there’s lots of HIV infection, the same logic probably applies. “But from the standpoint of extrapolating to parts of the world like the United States, it does raise questions,” he adds. “If it was new TB, the probability of acquiring a new bug in Haiti certainly would be much greater in Haiti than in the U.S.”

Still, if what researchers in Haiti were seeing was reactivation of old disease, “then the premise is that it’s going to recur when you’re immunocompromised. I don’t know the answer, but if you had someone here with HIV and they begin to deteriorate, then maybe you need to go back on INH. Whether it’s your own bug that will reactivate or whether you’ll contract someone else’s, you may be able to control a new infection. And you’ll get disease, whether it’s exogenous or endogenous.”

Relapses occur in HIV patients here, too

Indeed, American patients with HIV who kept either relapsing or succumbing to new TB infections provided part of the impetus for the study, Johnson says. “We started seeing occasional patients here, and they were also seeing them in Haiti,” he says. “These were patients who developed TB, who’d been treated and were doing well, but who developed TB again a couple of years later.” There have been other studies where researchers looked for the same effect but didn’t find it, perhaps because they didn’t follow patients long enough, Johnson adds. “We looked for 24 months after treatment,” he says. “We followed some patients even longer.”

Well, yes and no, says **Rick O’Brien**, MD, chief of research and evaluation branch of the Division for TB Elimination at the Centers for Disease Control and Prevention in Atlanta. “In a Zairian

study that was done five or six years ago, they saw the same thing,” O’Brien says. That study, structured along the same lines as Johnson’s, randomly assigned HIV-positive patients who’d finished their TB treatment to continue therapy with rifampin, isoniazid, or placebo. Comparing the entire HIV-positive group with a group of HIV-negative patients, those researchers found “no significance in relapse rates, and so they concluded that standard therapy [without any post-treatment prophylaxis] was fine,” explains O’Brien.

But an analysis of all the arms of that study turns up something else, he continues. Relapse rates among the HIV-positives on extended therapy turned out to 1%; among the HIV-positive on standard therapy, 9%; and among the HIV-negative group on standard therapy, 5%, he says.

That means there’s no statistically significant difference between the HIV-positive and HIV-negative groups, with their respective relapse rates of 9% and 5%, he explains. But by adding extended therapy, relapse rates dropped from 9% to 1% — a big difference. ■

Risk said lower for health care workers

Proper safeguards are the key

Research presented recently during a workshop at the Institute of Medicine (IOM) on regulating occupational exposure to TB suggests that health care workers are at a much lower risk for developing TB than experts had thought.

Workshop participants addressed the adequacy of current government guidelines for protecting health care workers against TB infection, looking at the potential for stricter measures from the Occupational Safety and Health Administration. Thomas Daniel, MD, a professor and researcher at Case Western Reserve University in Cleveland, told the committee that health care workers’ risk of contracting TB in the workplace has “declined significantly” in response to guidelines from the Centers for Disease Control and Prevention in Atlanta.

“In those health care facilities where modern infection control measures are in place, it now approaches the level of risk incurred by health

care workers in the communities in which they reside,” Daniels explained in his summary paper to the committee.

Keith Woeltje, MD, hospital epidemiologist at the Medical College of Georgia in Augusta, says the CDC guidelines of 1990 and 1994 were widely implemented by nearly all health care institutions, resulting in a dramatic decrease in TB infections.

Woeltje told the committee that the CDC guidelines are adequate and no further action is needed from OSHA. The CDC guidelines are effective because they are more flexible than the OSHA guidelines, he adds.

The CDC guidelines stress identifying TB patients and getting them into isolation quickly. The IOM conducted an additional closed meeting on regulating occupational exposure to TB in September and will announce its revised recommendations by January 2001. ■

False-positive TB tests: Is the reagent at fault?

Improper reading of skin tests also a problem

False-positive reactions to a tuberculosis skin testing reagent are causing a stir among employee health departments.

In one month after switching from Aplisol (Parkdale Pharmaceuticals, Rochester, MN) to Tubersol (Pasteur Merieux Connaught USA, Swiftwater, PA), 11 health care workers at the Grady Health System in Atlanta had a new tuberculin skin test (TST) conversion. Chest radiographs showed no evidence of tuberculosis, and retesting with the Tubersol purified protein derivative (PPD) came out negative.¹

Employee health and infection control professionals concluded that the false positives were the result of the switch.

In a letter to the *Journal of the American Medical Association*, **Henry Blumberg**, MD, an infectious disease specialist at Grady and the Atlanta-based Emory University School of Medicine, and colleagues disputed a recent published study concluding that Aplisol and Tubersol are equivalent.²

“Our experience demonstrates the need for a better and more reliable test for detection of

tuberculosis infection and suggests that when a TST is used among a low-risk population . . . the majority of positive results actually may be false-positives,” the letter stated.

Questions about false positives with Aplisol have lingered for years. Employee health professionals have reported itching and redness associated with the reagent. But does Aplisol produce an induration that is significantly larger than what Tubersol would produce in the same person?

According to a comparative study conducted by **Margaret Villarino**, MD, MPH, at the Centers for Disease Control and Prevention, and colleagues at CDC and state health departments, there were no significant differences between the reaction sizes of the two reagents when used in low-risk populations.³

Some tuberculosis experts assert that “false positives” actually stem from improper reading of the skin test reactions and not from a problem with the reagent.

In one study, pediatricians, pediatric academicians, and nurses were asked to read the Mantoux tuberculin reaction of a known tuberculin converter. Only 7% read it correctly.³

“People don’t know how to read them very well at all,” says **Lee B. Reichman**, MD, MPH, executive director of the National Tuberculosis Center at the University of Medicine and Dentistry of New Jersey in Newark. The National Tuberculosis Center provides training to hospitals and health departments across the country. “It’s very disappointing. If people are properly and appropriately trained and experienced, then you get better readings.”

Edward Nardell, MD, tuberculosis control officer at the Massachusetts Department of Public Health and associate professor of medicine at Harvard Medical School in Boston, agrees that the skill level of people reading the skin tests may have made a difference in the Villarino study. But he notes that employee health departments must conduct the tests in a time-pressured, real-world environment — not in a controlled study.

“I think you can train a research nurse or physician to tell the difference between a soft induration you get with Aplisol and the harder induration you get with Tubersol, and to ignore the erythema [redness]. You seem to get a lot more [redness] with Aplisol,” says Nardell, who also practices at Cambridge Hospital.

“I personally have seen an intern who was told

by employee health that she had a positive PPD, having previously tested negative,” he says.

“I looked at it and it was pretty impressive, with a lot of redness and some soft induration. I had her retested with Tubersol and there was no reaction at all. I think the majority of occupational health nurses and physicians would call that positive,” Nardell adds.

The Massachusetts Department of Health, which provides tuberculin statewide, is switching back to Tubersol, despite the increased cost of that reagent. That change includes the employee health department at Cambridge Hospital.

“We’re in a low-prevalence situation in most of the country for tuberculosis,” says Nardell. “The last thing in the world you want is an overly sensitive test.”

Reichman suggests that employee health departments using Aplisol focus on proper reading of skin tests. “They should choose an antigen — don’t change the antigen — and make sure it’s read properly,” he says. “You can’t compare people unless the antigen stays the same.”

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Dual infections complicate initiatives in Africa

Problem is growing in other areas

More than 34 million people worldwide are infected with HIV, and about one-third of them are co-infected with *Mycobacterium tuberculosis*. The dual infection has created a deadly and expensive dual epidemic, particularly in sub-Saharan Africa, where more than 24 million HIV-infected people reside.

International health organizations estimate that only about 20% to 25% of all TB patients worldwide have access to effective diagnosis

Community TB Care in Africa Project

Project site	Intervention cohort (community DOT option)	Control cohort (no community DOT option)	Type of control
Machakos, Kenya	90% (537)	85% (600)	Historical 1996
Lilongwe, Malawi	68% (1,455)	61% (914)	Historical 1997
Kiboga, Uganda	78% (135)	61% (148)	Historical 1997
Kawempe, Uganda	52% (298)	33% (unknown)	Historical 1997
Hlabisa, S. Africa	86% (37)	68% (638)	Concurrent
Guguletu, S. Africa	69% (548)	66% (82)	Concurrent
Ndola, Zambia	77% (40)	49% (59)	Concurrent

Source: Dermot Maher, Communicable Disease Control, Prevention, and Eradication, World Health Organization; TB-LIFE Meeting. Atlanta; Aug. 28-29, 2000. Percentages (and numbers) represent treatment completion of project participants.

and treatment provided under the directly observed therapy, short-course (DOTS) strategy, which is acknowledged to be the best TB control method.

In many countries in sub-Saharan Africa, up to 70% of patients with sputum smear-positive pulmonary TB are HIV-positive, and half of people with HIV develop TB. While precise statistics are not available, most international health officials agree that TB is the single leading cause of death among HIV-infected Africans.

HIV infection has made TB infection even more deadly by promoting rapid development of TB disease in people who are newly infected with TB or whose TB infection has been dormant, says **Dermot Maher**, BM, BCh, a medical officer with Communicable Diseases Control, Prevention, and Eradication of the World Health Organization (WHO) in Geneva.

Likewise, studies show that a person's immune response to *M. tuberculosis* infection enhances HIV replication and may accelerate the progression of HIV disease. Together, the two epidemics have spread misery and death across sub-Saharan Africa.

Cambodia and Thailand also bear watching

While WHO and other international organizations have been focusing on Africa — the region of the world in which the problem is the most critical — they've kept an eye on other potential hot spots. Cambodia and northern Thailand both have high HIV infection rates coupled with high TB infection rates, Maher says. "In those parts of India where HIV is more common, [there's a] risk of fueling the TB epidemic," he adds. "But in India, overall HIV infection rates still are relatively low."

But the dual TB/HIV epidemics in those Asian nations are dwarfed in comparison to sub-Saharan Africa's troubles.

"We've had the chance to observe over the past decade — and very many sub-Saharan African countries have seen — terrific escalations of TB due to HIV and poverty," Maher says. "A number of countries have seen their TB case rates go up threefold or fourfold."

Double whammy

The symbiotic way in which the two infections promote progression to disease and death also fuels the transmission rates. TB is not contagious when it's in a latent form, but because HIV infection causes people also infected with TB to progress rapidly from latent TB infection to full-blown TB disease, it also increases the pool of people who are contagious with TB and who are therefore spreading it to many others, says **Kenneth Castro**, MD, director of the Division of TB Elimination at the Centers for Disease Control and Prevention in Atlanta.

CDC researchers have found increased viral replication in lymphocytes and macrophages of HIV patients who have active TB. Co-infection with *M. tuberculosis* and HIV-1 resulted in a level of viral replication in cells 1,000-fold higher than that seen in a person infected with HIV alone, according to posters presented in June at the Tuberculosis 2000 conference in New York City.

All of the recent research and surveillance data point to a problem that will only escalate unless comprehensive measures are taken to stop the co-infection rate.

"Our responsibility is to declare this situation as intolerable, that the status quo is intolerable,

and it calls for action," Castro says. "If nothing is done, it's only going to get worse."

Until recently, health ministries and support organizations tackled each disease separately, rarely working together. WHO and others now recognize that this approach will not succeed. TB organizations need to collaborate with HIV organizations, combating the epidemics with a united front.

"To address the problem, you have to do two things to turn off the TB epidemic," Maher says. "You need to stop TB transmission by identifying and curing the infectious cases using the DOTS strategy, and you need to stop HIV transmission since HIV is fueling TB."

Good collaboration between HIV and TB programs, therefore, is key. In trying to make the solutions to stopping both epidemics widely available, the world's health community has some new initiatives that should help. WHO, the CDC, UNAIDS, USAID, and other organizations are promoting community-based initiatives aimed at providing testing, treatment, and counseling for people who may have HIV and TB.

While HIV antiretroviral treatment continues to be cost-prohibitive for most people and nations in sub-Saharan Africa, TB treatment is much more affordable, costing as little as \$10 to \$20. However, the same lack of health care infrastructure that makes HIV testing, counseling, and treatment so elusive in those nations also makes it difficult to treat TB patients successfully.

Patients need to adhere strictly to the TB medication, sometimes for as long as eight months, for treatment to succeed. Low adherence rates have been associated with a rise in drug-resistant TB strains in many countries. In the United States, this type of strict adherence has been possible among homeless and marginal populations when the drugs are administered in a direct observation therapy program.

A community effort

International organizations are working with health ministries in many countries in sub-Saharan Africa to ensure all TB patients have access to the type of support necessary to enable them to adhere to and complete therapy.

One such project, called "Community TB Care in Africa," is investigating how to engage community participation in tackling TB. Another initiative, called "ProTEST," is investigating how health officials and others may provide interventions

designed to prevent HIV infection from fueling the TB epidemic through voluntary counseling and testing for HIV and other measures.

The Community TB Care in Africa project, begun in 1996, is evaluating the community contribution to effective TB control in countries with high HIV prevalence. Projects based in districts of Botswana, Kenya, Malawi, South Africa, Uganda, and Zambia began implementing community TB

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care interventions in early 1998. Their chief intervention is DOTS for people with TB. WHO also provided technical support for community TB projects in Tanzania and Ethiopia. Most of the pilot sites have demonstrated high rates of treatment success.

Also, the program resulted in lower health care costs for the communities involved. The health systems saw cost savings of between 16% and 72%. The average length of stay for these TB patients dropped by 73% to 98%, and the average family costs also dropped substantially. In Kiboga, the district hospital closed its TB ward because all of the TB patients were successfully treated in the community, resulting in a considerable cost savings to the hospital, Maher says.

DOT in the parish

“Community member volunteers identified through the parish development committee were doing direct observation therapy,” he adds.

The ProTEST initiative is designed to develop a district-based model for the integrated delivery of health care services to reduce the burden of TB and HIV. ProTEST programs will attempt to reach some of the 90% of people with HIV who do not know they are HIV-positive.

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“The program is promoting testing for HIV to make sure those identified with HIV have access to preventive TB treatment if they don’t have TB yet,” Maher says.

ProTEST projects are under way in South Africa, Malawi, and Zambia. Uganda is expected to start a project later this year, and Zambia will combine this project with a project that looks at prevention of the transmission of HIV from mother to child. ■

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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