

# TB MONITOR™

The Monthly Report on TB Prevention, Control, and Treatment

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## IN THIS ISSUE

### IOM report says TB rule should be more flexible

Yet another development has occurred in the continuing drama over the Occupational Safety and Health Administration's proposed TB rule. The Institute of Medicine is offering some constructive criticism of OSHA's rule. In a report issued in mid-January, the IOM said the rule should be more flexible in how it categorizes risk settings, how it approaches the issue of skin-testing, and the manner in which respiratory protection is assessed and determined. The report cites new data that suggest some brands of respiratory protection devices on the market cannot be properly fitted and provide inadequate protection. . . . . Cover

### Cost of care for foreign-born patients is soaring

The cost of treating drug-resistant foreign-born patients is having a tremendous impact on TB budgets, experts say. Because these patients usually have no insurance, local governments often get stuck with the tab. For instance, two years ago, a small county in Washington state ended up paying for the treatment of a foreign-born patient who proved resistant to six drugs. The cost of treatment exceeded not just the TB control budget for the county, but the entire county budget. . . . . 15

### TB officials in California seek to revise funding model

California TB officials are advocating changes in public health care funding practices to replenish the dwindling pot of money available to treat indigent patients. They want to expand the state's Medicaid program to cover inpatient care, extend the definition of emergency care to include TB cases in which a cure is still pending, extend Medicaid benefits to undocumented aliens as well as to documented patients, and collect fee-for-service payments for directly observed therapy and other services performed in Federally Qualified Health Centers . . . . . 17

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## OSHA rule inflexible on some points, IOM says in new report

*'Balanced' report dishes out helpful criticism*

The proposed new federal TB rule may help protect health care workers and others in some settings, but it needs to be more flexible, concludes a new Institute of Medicine report on the subject.

The 350-page document, commissioned with a grant from Congress by partisans seeking to stop the U.S. Occupational Safety and Health Administration (OSHA) from going forward with the new standard, is titled "Tuberculosis in the Workplace" and was released Jan. 16.

"It is a consensus document, one in which we don't specifically address the case for or against a new OSHA standard," says IOM project officer **Marilyn Field, MD**. "That's not what we were asked to do; and considering that we weren't, and given the very limited amount of time available, we stuck pretty closely to our charge."

That charge was to assess the occupational risk for TB; to determine how closely employers are abiding by the Centers for Disease Control and Prevention's standards; and to weigh the likely impact of a new OSHA standard.

The IOM committee decided the risk of TB infection remains a problem for certain workers and in certain places, Field says. "Though occupational risk is declining, we found that vigilance is still needed in workplaces and communities," she says. At the same time, the report faults the proposed OSHA standard for not being flexible enough, she adds.

The committee found three areas in which the rule should be more flexible, she says:

- the way a risk setting is categorized;
- the way the OSHA document approaches the issue of skin-testing;
- the way the need for respiratory protection is assessed and determined.

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**Elite TB center undergoing fundamental changes**

It's been a rough several years for TB officials at the National Jewish Medical and Research Center in Denver. The hospital's mycobacterial section, long acknowledged as a court of last resort for TB patients with intractable disease, has been downsized; collection rates from indigent patients have declined; costs have soared; and the center's emphasis has begun shifting toward treatment of childhood asthma and cystic fibrosis. But recent positive changes have encouraged the head of the mycobacterial service to believe that the TB program will not only survive, but will flourish . . . . . 18

**U.S. support lacks gusto at latest G-8 confab**

Europeans seemed to emerge from the latest G-8 meeting with a plan in hand to combat TB, but U.S. representatives were less assertive, according to reports from the meeting in Japan. While the Europeans and Japanese appear to be mounting a more aggressive plan of action, one official says the U.S. seems have adopted a more laid-back attitude and is willing to wait for drug companies to solve pharmaceutical problems . . . . . 19

Journal Reviews

**Travel: TB or not TB? That is the question**

Travel allows exposure to other cultures. It may also allow exposure to other diseases. The data presented in this study suggest the risk of acquiring TB in long-term travelers was significantly greater than the reported risks of travelers to developing countries of acquiring cholera, malaria, or meningococcal disease, but comparable to that of acquiring hepatitis A virus infection. Children who travel may be at even greater risk than adults . . . . . 21

**Update on rifamycins in TB and HIV**

Patients concurrently infected with HIV and tuberculosis present complex care issues for clinicians, not the least of which are the selection of an optimal regimen for both diseases and the management of drug interactions. Earlier guidelines recommended against the use of rifampin in patients receiving protease inhibitors or the use of rifabutin in any patient receiving ritonavir or delavirdine. Based on newer pharmacological data, the March 10 issue of *MMWR* presents newly modified recommendations for the use of rifamycins in HIV-infected patients . . . . . 24

**COMING IN FUTURE ISSUES**

- How the IOM wants to change the TB rule
- What's up at Ten Against TB?
- New diagnostic tools are coming
- Tracking source cases for kids
- CDC ponders new guidelines for health care workers

In the area of categorizing risk, the OSHA proposal lacks the requisite subtlety to deal with the variety of situations that exist. "The CDC has five categories of risk, ranging from high to minimal, but OSHA essentially recognizes only two," Field says. By that reckoning, an institution that falls into the "low-risk" category needs to do very little to protect its workers from TB; on the other hand, institutions that fall into the so-called "high-risk" category must do quite a lot, Field notes. A more appropriate scheme would take a more flexible approach, depending on where institutions fall along a spectrum of risk.

When it comes to skin-testing, Field says the committee readily acknowledged that old CDC guidelines reflect concerns of a bygone era and were formulated in the wake of several TB outbreaks. The biggest concern with skin-testing now is that testing too much may elicit false-positive reactions, she adds. "We concluded that even though skin-testing is not something the OSHA standard can't deal with, we were still worried about [the standard's lack of] flexibility."

Finally, OSHA also needs to revisit its recommendations for respiratory protection, Field says the committee concluded. On one hand, she says, the committee felt the OSHA standard should have been more explicit when it came to certain high-risk occupations, such as those that require performance of autopsies and bronchoscopies, and that the standard ought to insist on high levels of protection in those settings.

On the other hand, she adds, hospitals or other facilities in which there is only an occasional case may be adversely affected by the burden of having to implement respiratory protection programs, because such programs can "divert resources" from areas of greater need, says Field.

The report cites new data that suggest some brands of respiratory protective devices on the market cannot be properly fitted and provide inadequate protection, Field says.

Most of the available data pertaining to the effectiveness of respiratory protection come from animal studies or laboratory modeling, she adds. What data there are do offer support for the CDC concept that administrative controls take precedence over engineering controls, which in turn should take priority over respiratory measures.

One of the most interesting parts of the report may be the piece that examines new evidence from tests of various respiratory protective devices. Some manufacturers' equipment has been found not to seal effectively, Field says. "For some of

these models, people couldn't get a good fit so the equipment did not leak unacceptable amounts of air," she says. "We felt [government agencies] should be attending more closely to the manufacturing process."

To order or view the report, readers may call the IOM at (800) 624-6249, or they can visit the National Academies of Science Web site at [www.nap.edu/catalog/10045.html](http://www.nap.edu/catalog/10045.html). The report should be available as a hardcover document by early spring. The cost is \$49, and the report is offered at a 20% discount to those who order on-line. ■

## High cost of MDR-TB has controllers concerned

### *Could states set up contingency funds?*

The high cost of treating foreign-born patients with drug resistance is taking a heavy toll on state and local TB programs, say program administrators across the country. Whether or not such patients are documented, they're often ineligible for traditional funding sources such as Medicaid. At the same time, they're more likely than U.S.-born patients to have expensive resistant strains of TB, many programs directors say.

To help underwrite the costs, some TB controllers are contemplating such distasteful steps as cutbacks in services and charging patients for the cost of their medications.

"These programs are saying they need help," says **Walter Page**, executive director of the Atlanta-based National TB Controllers Association. "They're saying the cost of treating these patients is busting their budgets."

"We can usually handle these [foreign-born] cases when they're not multidrug-resistant," says **Ellen Mangione**, MD, Colorado's TB control officer. A TB strain is classified as multidrug-resistant (MDR) when it has resistance to both isoniazid (INH) and rifampin. "But many of us are seeing more and more MDR. We have two such cases right now, and it's enough to put us into discussion about discontinuing other program activities, such as treatment for those with latent TB infection."

And that, she adds, doesn't bode well for the future, because today's latently infected patients, if left untreated, will provide tomorrow's cases.

Others in Mangione's shoes echo the same complaint. "It's true that we have fewer TB cases overall, but the ones we do have tend to be sicker and harder to treat," says **Kimberly Field**, RN, head of TB control in Washington state. In 1999, for example, Washington recorded five cases of MDR-TB, compared to 1998, when there were none, or to the entire period from 1993 to 1997, when there were just three.

The cost of treating such cases can be astronomical, Field adds. Two years ago, she says, a rural Washington county got stuck with the tab for treating an undocumented foreign-born patient who proved resistant to six drugs. The cost of treatment exceeded not just the TB control budget, but the entire county budget, she adds.

"The impact of a single case of MDR can be very dramatic in a small county," says **Ram Koppaka**, MD, chief of TB control in Virginia and the Centers for Disease Control and Prevention technical officer for the state. "A local jurisdiction's budget for TB control might be very small, so it doesn't take much to break that budget."

Even cases that don't qualify as multidrug-resistant can run up high costs, notes **Nancy Baruch**, RN, MS, MBA, Maryland's TB control officer. "Increasingly, we're seeing more of other kinds of patterns of resistance as well, including resistance to INH alone, or to INH and some other drug, such as streptomycin," Baruch notes. "Once you've lost INH, right there you've already increased the cost of treatment."

### *Mississippi eyes charging patients for meds*

In Mississippi, TB control officer **Mike Holcombe**, MPA, says he's contemplating a step he dreads taking. To scrape up money to treat foreign-born patients among his refugee populations, he's thinking about trying to collect from Medicaid and third-party insurance programs — which translates to extracting payments and copayments from patients for their medications. "It's exactly the opposite of what we want to do," he adds. "But to get reimbursement from Medicaid and insurance, you have to find a way to collect," he says. "Essentially, what this means is we may have to penalize other patients in the program in order to subsidize the refugee program."

What really smarts, many TB controllers add, is that those who make the decision to place refugees or to admit immigrants seem clueless

about where, exactly, the public-health buck stops.

“People outside TB circles seem to assume that when a refugee or immigrant enters the country with TB, ‘someone else’ will take care of the problem,” he says. “They also assume that public health resources will automatically be made available to these people, and that public health in its current format will be able to go on absorbing these costs indefinitely. But ultimately, the problem belongs to the local TB program, and that local program has nowhere else to go.”

Often, small local programs hit with an MDR-TB case for the first time are shocked to find they can’t simply go to the state program and get bailed out, Field says. The trouble is that the CDC expressly forbids the use of categorical funds to pay for medications. “That often comes as a shock to people when they find out that’s the case,” she adds.

As for Medicaid — available in theory to anyone with a positive TB skin test — those funds are available only if states sign up and agree to put forward their part of the matching funds, says Holcombe. “Agencies assume that if someone isn’t eligible for Medicaid, that they can get refugee assistance funding,” he adds. But he’s found out the hard way that such funds are available on the same basis as Medicaid, so a refugee who isn’t eligible for one isn’t going to be eligible for the other.

### *It’s all about fairness*

Leaving local programs holding the bag strikes Holcombe and others as patently unfair. “If these folks arrive with no other funding available, and the State Department has let them come in, then I believe that the money for treating them should come out of State Department dollars,” Holcombe says.

It’s not a question of wanting to keep out foreigners, Koppaka adds, but of providing for their care in a reasonable way. “If you’re a member of a refugee group, then you’ve got nowhere else to go, and you belong here,” he says. “Still, people should give some thought about where the money will come from to treat these people. Is it fair to add that to the burdens of a local program, or should there perhaps be a national procedure to ensure treatment will be provided?”

One idea would be to establish some sort of trust fund for the treatment of such patients.

Getting the feds to agree to foot the bill for such a program would take a major change in CDC policy because categorical money can’t be used to pay for TB medications.

That idea gets a chilly reception at the CDC. “The best way to deal with MDR-TB is to treat ordinary TB appropriately,” says **Zack Taylor**, MD, new chief of the Field Services Branch at the CDC’s Division of TB Elimination. “We could get drawn into pouring a lot of money into treating MDR, and before you know it we’d be spending half our budget on it. Personally, I think CDC’s best strategy is to fund strong TB control programs.”

That leaves MDR treatment up to individual states, or perhaps regions. In Washington State, a working group created the same year the state got hit with four MDR cases has been pitching just such a notion to the state lawmakers, says Field. The proposal has been presented twice, but so far hasn’t gotten anywhere, she adds — partly, she thinks, because other measures tacked onto the package distracted lawmakers from getting the real picture.

More money would help, but that’s not the only thing lacking, says Holcombe. Better notification and screening would go at least partway toward solving his headaches, he adds.

Take a recent episode involving a group of refugees from Kenya. Holcombe says he heard first that about 20 Kenyan “boys” would be arriving in Mississippi soon. That figure then changed to 40, then 50, and then 80. As the refugees began trickling in, it became clear that some of the “boys” were in fact adults, many of them toting newborn babies.

Meanwhile, paperwork on the Kenyans drifts in periodically to Holcombe’s desk, announcing that another handful of Kenyans arrived several weeks ago. That means that with luck, the refugees will still be where they’re supposed to be once TB control field workers catch up with them. With more luck, all they’ll need will be treatment for latent infection, not active disease or disease complicated by resistance.

Past experience with this kind of situation has made Holcombe less than optimistic, he adds. “I believe something needs to happen at the national level to modify both notification and screening procedures,” he says. “The State Department knows when these people are coming - they don’t just materialize out of thin air. Why can’t they tell us when they’re coming? We shouldn’t be getting notifications after the fact.”

Knowing beforehand at least would give him time to move extra personnel around, if needed, and would prevent refugees from moving on before TB investigators can locate them.

Screening needs to be tightened, too, Holcombe says, especially if more money for treatment is not forthcoming. Shortening the interval between the time an immigrant is screened and the time he or she is allowed to enter the United States is one much-needed step, he says. So is putting in place a better set of proficiency standards for those doing the screening. "I know that only a relative few slip through with active disease," he says. "But why should there be any? Why should I have one? Why should Carol Pozsik [the TB controller in South Carolina] have one?"

In Maryland, Baruch says she's been able to juggle her expenses by shifting the costs of some

patient care to a state facility, where the TB program traditionally sends both MDR cases and co-infected patients. Trouble is, the state facility has begun to balk at the high cost of treating these patients. For two weeks last month, in fact, it refused to take any such patients at all. With a temporary reprieve under her belt, Burr says she's breathing easier these days.

But for the long run, TB controllers say, it's going to take something more. Back in Washington, Field recounts an eye-opening visit she made recently to an electronics plant, where skin-testing was under way for 700 co-workers of a foreign-born patient with highly infectious TB. "I met people who were working there who were from Russia, Bosnia, Mexico, China, and Korea," she marvels. "To me, that says this trend will continue — and the issue we'll be dealing with will be the cost." ■

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## California aims to tap more Medicaid gushers

*Hiring retired HRSA staffer was first step*

**T**B control programs struggling to pay for foreign-born patients with multidrug-resistant TB are watching California with especially keen interest these days.

Already known for their wizardry in tapping into Medicaid funding — the program goes by the name of MediCAL in California — state TB controllers in California are now considering how best to drill for additional Medicaid gushers.

Already, certain jurisdictions in the state have better-than-average success in enrolling eligible TB patients into Medicaid, rendering local jurisdictions eligible for reimbursement on a fee-for-service basis for directly observed therapy and directly observed preventive therapy. At \$19.20 a visit, that's not a bad start.

Also, under the present arrangements (in California as elsewhere), local jurisdictions can get paid for inpatient care for "emergency" patients — but only assuming the MediCAL program can be persuaded that the patient is truly an "emergency." That sounds good in theory, but proves a tough sell in practice, most TB administrators say, because it means they have to convince a hospital to take a patient on the off chance that the patient will be deemed an emergency at some point.

What the California TB policy wonks want now are three more things, says **Stuart McMullen**, the senior public health advisor assigned to the state TB control program.

First, he says, they're working to expand MediCAL benefits to cover inpatient as well as outpatient care. That would fill the gaps for someone who needs to be hospitalized but who doesn't qualify for "emergency" status.

Second, the program wants to expand the definition of "emergency" to cover all TB cases in which a cure is still pending.

Third, it wants to extend MediCAL benefits to undocumented patients as well as documented patients.

Finally — and most promising, perhaps — the program is considering collecting fee-for-service reimbursement for directly observed therapy and other outpatient services performed in a specific setting: namely, places known as Federally Qualified Health Centers (FQHCs).

As McMullen explains it, any local jurisdiction can declare itself an FQHC if it's willing to tackle the paperwork, which includes enumerating all reimbursable costs and all patient visits and then divvying them up so as to arrive at a reimbursement rate for each center.

The good news, as it turns out, is that the FQHCs in California haven't been billing for outpatient services performed by many staff members, even though they apparently can start doing so, McMullen says. How did this oversight occur? It seems the health centers can legally bill

the feds only for patient visits performed by either a physician, a physician assistant, or a nurse practitioner. Thus, the bean-counters at the centers had duly not billed anyone at all for costs of their clinic nurses and field workers.

But it would be perfectly legal for the centers to seek reimbursement under the old fee-for-service arrangement, adds McMullen, which is exactly what he hopes MediCAL officials will start letting them do.

It's a scheme that ought to work for any state where there are FQHCs, he says. "The only caveat here is that the health centers can't use state or federal money to hire these outreach workers, since that would be double-dipping," he points out.

The real question may not be whether the Californians will score hits on all these fronts, but how they were so clever as to think them up in the first place. It turns out that the answer to that one is easy.

"We found a retired guy from HRSA," the Health Resources Services Administration of the federal Department of Health and Human Services, McMullen says. "And we hired him. He's been sorting all this stuff out for us."

Even with such a resource at hand, dealing with Medicaid isn't an easy proposition, McMullen admits. It's extremely complicated; plus, the social service workers whose task it is to guide patients through the mountains of paperwork are often ticklish about spending lots of time cooped up with a TB patient, he says.

To keep jurisdictions on an even keel, the state offers periodic inservice training sessions in how to deal with the Medicaid beast.

For the rest of the world -- or at least for programs that can't find their own retired HRSA staffer to hire -- TB controllers who want to know more about how Medicaid works can contact McMullen, he says. ■

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## Brighter days ahead at National Jewish

*Service finding new focus, fresh energy*

For the elite corps of TB experts at National Jewish Medical and Research Center in Denver, recent years have brought some tough times.

The hospital's mycobacterial section, long acknowledged as a court of last resort for TB patients with intractable disease, has been downsized. Collection rates from indigent patients, never substantial, in recent years had dwindled to a trickle — even as the cost of treating multidrug-resistant disease took off into the stratosphere.

In its upper echelons, the hospital's administration was unflagging in its pledges of support; but starting as long as a decade ago, the focus clearly had begun to shift from the antique-sounding disease toward childhood asthma and cystic fibrosis.

Even so, the prevailing mood here these days is one not of defeat, but instead determination and optimism. "I believe we will not only survive, we will prosper," says **Michael Iseman**, MD, chief of mycobacterial service in the hospital's pulmonary section.

For one thing, Iseman says, the new scaled-back arrangement — one in which he voluntarily took a pay cut so the hospital could maintain a

strong clinical service — has given Iseman more time to pursue grants and do research. He and other long-timers say they are also thrilled at the recent addition of a new staff member, Mary Ann DeGroote, MD, a Fulbright scholar with impeccable credentials and a high level of enthusiasm.

The mycobacterial section also has begun staking out a new area of expertise: the treatment of disease caused by nontuberculous mycobacteria, also known as atypical mycobacteria. Although there exists no national patient registry for atypical mycobacteria, available evidence suggests infections due to atypicals are on the rise, many TB experts say. "It's almost as if there is a population of vulnerable people, and when TB recedes, the atypicals come in to take its place," says Iseman.

Along with new energy and focus, revenues are now up, too. Philanthropic giving from families and descendants of patients whose lives were saved here decades ago has risen by 50%. Patient referrals are also beginning to rise, perhaps thanks to a shift in the mindset of HMOs, where gatekeepers who once may have been reluctant to send patients to costly centers of expertise are newly chastened by a string of recent lawsuits that have levied steep penalties against HMOs.

Then there's research. After years of trying unsuccessfully to build a bridge to the hospital's highly-regarded T-cell biology research unit, Iseman says he now senses interest there.

Outside National Jewish, however, a sense of bitterness lingers. “Mike Iseman is a national treasure,” says **Lee Reichman**, MD, MPH, director of the National TB Center at the New Jersey Medical School in Newark. “They ought to give the man a chauffeured limousine and a gold-plated desk. Instead, he takes a pay cut and goes on half time. It’s a disgrace.”

National Jewish was founded in 1899, nestled in the front range of the Rocky Mountains. The mountains set the stage for the establishment of a host of other TB sanitariums, as well. Most of these sprang up to serve a clientele of well-to-do middle-class denizens of the East Coast, thousands of whom boarded stagecoaches and railroad cars to come west, hoping to find a cure in the pristine mountain air.

Unlike the rest, National Jewish declared its mission was to serve patients who could not otherwise afford to pay. From the day it opened until the mid-60’s — the decade that saw the creation of government-sponsored insurance programs for the poor — the hospital’s dictum was: “None who enter shall pay, and none who can pay shall enter.”

The descendants of TB patients who benefited from treatment at the hospital in those early years form the core of an energetic contingent of fundraisers. Though there are individual donors among them, there are also several industry and trade associations based in New York City and Los Angeles that sponsor annual dinners every year, raking in as much as a million dollars a pop. Taken together, gross contributions amount to some thirty percent of the mycobacterial section’s annual budget. Nor has support dwindled as U.S. TB rates have fallen; to the contrary, Iseman says he’s certain that donors take pride in knowing they’re helping combat one of the principal scourges of the developing world.

The tradition of philanthropic giving means the hospital still maintains a “scholarship” fund for patients who can’t pay; the trouble, as any TB controller knows all too well, is that the cost of treating even a single case of multidrug-resistant TB can be staggering, often as much as \$250,000. In instances when patients are eligible for Medicaid, the hospital may collect a paltry \$0.25 on the dollar; but in many such cases, patients are simply admitted as “self-paid” — a euphemism understood to mean there will be no payment.

With numbers of MDR-TB down nationwide, Iseman is philosophical about what the future holds. “MDR-TB may have been our stock in

trade in the past,” he says. “But clearly, it’s not the future of the program.”

The upshot is that a lot of the TB work that still goes on here is a labor of love and is carried out on a strictly pro bono basis. Until recently, Iseman and his colleague Gwen Huitt, MD, took turns fielding the approximately 2,500 calls that come in every year from patients’ families and physicians. To ease the crushing load, they applied for a small grant to fund two nurses whose job is to screen and organize calls. Now, the two physicians divide about 600 consults between them, but the workload is still enormous, and both physicians lug work home with them at night.

Several years ago, when morale was at a low point, the beleaguered mycobacterial section went looking for a new home at the University of Colorado in Denver. In many ways, the match would have been a good one, because the university houses not only Marvin Pomerantz, MD — chief of thoracic surgery at the university, and the surgeon who performs the lung resections many MDR-TB patients eventually require — but also a cadre of local and state TB experts who often refer patients.

But at the time, the university was beset with troubles of its own, in the shape of an internal squabble over whether to pack up and relocate to a huge parcel of land bequeathed to the institution on the outskirts of town.

To Iseman, the deal began to look “like a first-class berth on the Titanic,” he laughs; eventually, talk of moving elsewhere died down.

These days, in any case, Iseman says he is content. “This, not somewhere else, is going to be my last stand,” he says. “You know, my mother was Irish,” he adds. “I’m not one to give up.” ■

## At G-8 follow-up meeting, U.S. takes low-key role

*Meanwhile, EU, Japan carry on without us*

**A**t December’s meeting of the G-8 in Okinawa, Japan, countries and organizations came together with the aim of figuring out how to plug in the rhetoric generated at the G-8 Summit back in July.

Reports from the follow-up suggest that the European Union, in particular, returned with a solid plan of action in hand, says **Ellen ‘t Hoen**,

a Dutch lawyer who provides legal counsel for the Medecins San Frontiers (known in the United States as Doctors Without Borders) Access to Essential Medicines Campaign. The campaign has pushed hard for lower prices for existing drugs and more money to spur development for new drugs.

At a July summit, the European Union and Japan had both made substantial financial commitments to fighting TB, malaria, and HIV/AIDS. The United States, by comparison, had promised only modest amounts of help.

“The EU council resolution is now moving into an action plan with a big budget, and the plan looks quite promising,” she says. “More than just money, there are concrete plans and research activities.”

The Americans were comparatively low-key at the follow-up meeting, adds ‘t Hoen. “There wasn’t much in the way of a concrete commitment” at the second round, she says. She added that Americans at the meeting still appear to subscribe to the belief that the pharmaceutical industry, left to its own devices, will eventually get around to fixing problems on their own.

“What the U.S. doesn’t seem to acknowledge is that the market is failing for people in poor countries, and that it will continue to do so,” she says. “That’s why you need active government involvement and public investment. We were very disappointed.”

### *So much for the next four years*

Whatever participants at the follow-up meeting may have been thinking, they refrained from confronting the Americans, says ‘t Hoen, because U.S. election results were still up in the air at the time of the conference. “We didn’t know what kind of U.S. we were talking about,” she says. “Now, we do — one in which increased investment for drugs that will benefit people in Africa and Asia looks bad.”

The trouble with a revved-up EU and a laid-back United States is that the combination won’t be enough to move drug research forward at the speed it ought to be going, says ‘t Hoen. “The EU and Japan can’t do this alone,” she says. “What we really need is global solidarity and support, and we don’t have that yet.”

One thing the Americans could do right away is to put some money into the Global Alliance for TB Drug Development, she points out. So far, the only contributor to the alliance has been

Microsoft founder Bill Gates, who gave the organization \$25 million in start-up money.

Still, ‘t Hoen concedes, there is reason for continued hope. This July, when the G-8 is scheduled to hold its next general meeting, infectious diseases will be back on the agenda. That in itself is a step forward, ‘t Hoen adds. ■

## Alliance selects grant proposals

The Global Alliance for TB Drug Development has begun going through a stack of letters from researchers around the world who are interested in making a formal application for alliance funding.

About 90 letters offering a brief description of proposed projects and research have arrived so far, says **Rick O’Brien**, chairman of the alliance’s Scientific Advisory Committee. Those letters, responses to notices the alliance has placed in journals and elsewhere, “are about the number we’d been expecting to get.”

Now, O’Brien’s committee must select the most promising projects and ask for full proposals. Final decisions on who gets to submit proposals should be made this month, he says.

## Correction

In the December issue of *TB Monitor*, an error occurred in an article describing research published by Henry Blumberg, MD, associate professor of medicine in the division of infectious disease at Emory School of Medicine in Atlanta. The work concerned false-positive tuberculin skin tests that had occurred at Grady Memorial Hospital in Atlanta. The article should have stated that after the hospital switched from Tubersol to Aplisol, the researchers determined that there were false-positive reactions to Aplisol among health care workers. In addition, the article contained an error in the reference for the publication, which should have read: Blumberg HM, et al. *JAMA* 2000; 83:2793. We regret the errors. ■

The Global Alliance is a consortium of public and private stakeholders that was formed to spur the development of novel anti-TB drugs. Under the prevailing market-driven system, only a single new anti-TB drug, rifapentine, has been approved for TB treatment in the past 20 years. ■



## Travel: TB or not TB? That is the question

**Synopsis:** The risk of tuberculosis in long-term travelers to developing countries is significant.

**Source:** Cobelens FGJ, et al. **Risk of infection with *Mycobacterium tuberculosis* in travellers to areas of high tuberculosis endemicity.** *Lancet* 2000; 356:461-465.

Cobelens and colleagues examined the risk of infection with *Mycobacterium tuberculosis* in adults traveling for three to 12 months to countries with an annual incidence of tuberculosis of 1% or more. Significant underlying illness, prior evidence of tuberculous infection, and prior bacille Calmette-Guèrin (BCG) vaccination were among the exclusion criteria.

Twelve infections were detected among 656 subjects who were skin-tested both prior to travel, which lasted a median duration of 23 weeks, and after return. Only two of the 12 had evidence of clinically active pulmonary TB. The incidence of tuberculous infection was 3.5 per 1,000 person-months of travel, while the incidence of active TB was 0.6 per 1,000 person-months. The incidence was highest in health care workers; among those with direct patient contact, it was 9.8 per 1,000 person-months. Non-health care workers had an incidence of 2.8 per 1,000; this was calculated by Cobelens et al to be approximately equivalent to an annual incidence of 3.3%.

*Comment by Stan Deresinski, MD, FACP, clinical professor of medicine, Stanford University:*

Travel allows exposure to other cultures. It may also allow exposure to other diseases. I still

recall with dread a taxi ride in Bangkok — being interminably stuck in traffic with a driver who could not stop coughing. Fortunately, I did not convert my PPD as a result.

In the United States, the annual incidence of TB in 1998 was 6.8 per 100,000 population. In contrast, the World Health Organization's estimates of TB case rates per 100,000 population in 1995 were: 241 in southeast Asia, 140 in the western Pacific, 242 in Africa, 168 in the eastern Mediterranean, 123 in the Americas (except the United States and Canada), 47 in Eastern Europe, and 23 in Western industrialized countries and Japan.

The data presented by Cobelens et al suggest the risk of acquiring TB in these long-term travelers was significantly greater than the reported risks of travelers to developing countries of acquiring cholera, malaria, or meningococcal disease, but comparable to that of acquiring hepatitis A virus infection.<sup>1-5</sup> The latter is estimated to be three per 1,000 travelers per month among unprotected travelers, including those who stay in luxury hotels, but is almost seven times greater among those who eat and drink under poor hygienic conditions.<sup>5</sup>

Children who travel may be at even greater risk than the adults studied here. U.S.-born children who traveled to countries with a high prevalence of TB in the previous 12 months were 4.7 times (95% CI, 2.0-11.2) more likely to have a positive tuberculin reaction than those who had not traveled.<sup>6</sup> In addition, children who had a household visitor from a country having a high prevalence of TB were 2.4 times more likely to have a positive skin test than were those who did not have a visitor (95% CI, 1.0-5.5).

Another important issue to the estimated 2 billion (or more) passengers who will fly annually by 2005 is the potential for transmission of TB during air travel.<sup>7</sup> The CDC has reported seven investigations involving one flight attendant and six passengers with infectious TB, more than 2,600 potentially exposed passengers and crew, and a total of 191 different flights.<sup>8,9</sup> There was, however, evidence of transmission in only two episodes. In one, evidence of transmission from the flight attendant to other crew members was found for those with 12 or more hours of exposure while working with the flight attendant with TB. Evidence of transmission from passenger to passenger was only found for a few passengers who were seated in close proximity to the passenger with active TB and only on one

flight of more than eight hours duration. No secondary cases of active TB were identified in any of the investigations.

The Canadian Public Health Service has made the following recommendations for prevention of TB in travelers:<sup>10</sup>

1. All travelers to high-prevalence countries, particularly those traveling or living overseas with children, should be informed of the risk of TB.

2. Travelers with significant immune compromise, such as HIV, should be informed of the serious risk associated with TB exposure and of the important limitations of either a BCG vaccination or periodic skin-testing with chemoprophylaxis in the event of conversion.

3. Travelers should be advised to avoid consumption of unpasteurized milk, because it may contain *M. bovis* or other pathogenic organisms.

4. Medical assessment of domestic workers or other host-country nationals who are in close contact with the traveler or the traveler's family, particularly if a chronic cough is present, may reduce the risk of TB exposure as well as potentially benefiting the local person involved.

5. Those working in health care settings in developing countries should follow current infection control recommendations to the greatest degree possible to minimize the risk of exposure to TB.

6. Travelers going to high-prevalence countries for extended periods (e.g., three months or less, if risk is expected to be high) or working in a health care setting in a developing country for any period of time should be offered a TST with five tuberculin units of purified protein derivative (including two-step testing where indicated) unless there is a past history of tuberculosis or a well-documented previous positive TST.

7. If the initial TST is found to be positive, current management guidelines should be followed.

8. If the TST is negative, the individual should be informed about practical means of avoiding TB exposure. Persons should be advised to choose either BCG vaccination or a TST at least every two years, but preferably annually, as well as three to six months after leaving the high-prevalence area. If a TST becomes positive, the traveler should be assessed by someone with expertise in TB to consider the use of chemoprophylaxis and to determine the chemoprophylactic regimen.

9. In making the choice between BCG vaccination or periodic skin testing with prophylaxis in

the event of conversion, the following factors should be considered:

- anticipated feasibility of, and compliance with, repeated skin-testing and chemoprophylaxis;
- likelihood of isoniazid intolerance (age, liver disease, excess alcohol use);
- likelihood that an infecting strain of *M. tuberculosis* may be isoniazid-resistant (depends on local rates of primary resistance);
- individual preference;
- age — the role of BCG vaccination may be particularly important in children, especially those younger than 1 year of age.

10. Where possible, BCG should be administered at least four weeks before the anticipated exposure to TB.

11. A "baseline" measurement of the tuberculin reaction three months after BCG vaccination may be considered to aid in the interpretation of any subsequent TSTs.

12. Regardless of the duration of travel or the preventive measures used, TB must be considered in the differential diagnosis of illness in travelers returning from high-prevalence countries as well as in immigrants from those countries.

The emphasis on BCG in these Canadian recommendations is greater than would be seen with U.S. recommendations. However, it seems reasonable that infants who will be staying in a country with a high prevalence of TB are candidates for BCG vaccination.<sup>11-13</sup> Vaccination may also be considered in health care workers, although the potential value of this approach is less certain.<sup>14-15</sup>

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# The tale of a long trail: Paris is Burning, Part II

Source: *MMWR* 2000; 49:317-320.

Some of you may have seen the documentary film *Paris is Burning*, which is about groups of transgender males who form closely knit social networks, or "houses" (although they do not necessarily live together) and who participate in runway fashion competitions called "balls." Public health investigators are reporting an outbreak of TB within such transgender networks in Baltimore and New York City, with the potential for spread to similar networks in other major urban areas.

Beginning in May 1998, active TB was diagnosed in four young black transsexual men, all of whom were HIV-positive and worked as prostitutes in the Baltimore area. Further investigation revealed that the men were part of a network of transgendered people in Baltimore, many of whom traveled to New York and other cities to compete in balls.

By identifying members of the network, 22 additional cases of TB in Baltimore and New York were eventually identified. Twenty-four of the 26 cases were confirmed by culture, and 23 had an identical DNA fingerprint.

Remarkably, standard contact tracing, whereby case-patients named contacts, was insufficient, resulting in the identification of only 14 individuals at risk. Rather, health officials were able to identify and screen an additional 91 contacts by developing profiles of the social networks, tracking individuals and their activities, doing home-based investigation, and by attending some of the actual balls and social events.

Through these more intensive efforts, it was also determined that several case-patients had traveled to New York, as well as other cities on the East Coast, to compete in balls. DNA fingerprinting of TB organisms from young black men in New York City found four additional cases that matched the Baltimore strain.

Because all TB isolates in New Jersey are typed, an additional case matching the Baltimore cases was identified. That patient was a young transsexual who had traveled frequently to Baltimore to participate in balls.

Several points can be made regarding this outbreak. It occurred among a group of young, highly mobile men who exist within a poorly

understood but closely knit social network of transgendered people. Many were HIV-infected, increasing the risk for active TB and transmission of disease. Many were also commercial sex workers, increasing the potential for widespread transmission of infection. Finally, standard case identification was inadequate in determining the extent of the outbreak. Instead, a sophisticated blend of laboratory investigation through DNA

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## Editorial Questions

For questions or comments, call Alice Alexander at (404) 371-8067.

strain typing and psychosocial/behavioral investigation necessitating a greater understanding of the social behaviors of this community was required.

There is a parallel between this investigation and the current investigation in San Francisco of an outbreak of syphilis among people who made anonymous sex contacts through the Internet. How do you trace potential contacts who exist in the demimonde, known only by their call names or Internet handles? Successful investigations like these are increasing requiring an understanding of the behaviors of these groups of individuals, which requires costly and time-consuming efforts on the part of individuals in local health departments manning the front lines of public health. State officials should keep these outbreaks in mind when evaluating public health budgets. ▼

## Update on rifamycins in TB and HIV

Source: *MMWR* 2000; 49:185-189.

Patients concurrently infected with HIV and TB present complex care issues for clinicians, not the least of which are the selection of an optimal regimen for both diseases and the management of drug interactions. Earlier guidelines recommended against the use of rifampin in patients receiving protease inhibitors or the use of rifabutin in any patient receiving ritonavir or delavirdine.

Based on newer pharmacological data, the March 10 issue of *MMWR* presents newly modified recommendations for the use of rifamycins in HIV-infected patients. Rifampin can be used for the treatment of active TB in patients receiving an efavirenz- or ritonavir-containing regimen, or in patients receiving the combination of ritonavir and saquinavir. Rifabutin can be used in patients receiving efavirenz or ritonavir, but the dose should be increased to either 450 mg or 600 mg daily with the former agent and decreased substantially to 150 mg two or three times weekly with the latter. The dose of rifabutin does not require modification if used with saquinavir (soft gel) as a single agent.

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The use of rifamycins in patients receiving other antiretroviral regimens remains uncertain, but patients with active TB should generally receive a rifamycin-containing regimen whenever possible, even at the expense of more potent antiretroviral therapy. Should this not be possible, an antituberculous regimen containing no rifamycin can be considered. The *MMWR* article also stated that the management of these patients requires the active input of a physician with expertise in the management of both of these diseases. ■

### 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. ■