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IN THIS ISSUE

In This Issue **continued on next page**

IOM report weighing new federal TB rules called 'consensus' document

Not expected to come down hard against OSHA regs

The Institute of Medicine's new report on the impact of proposed federal regulations aimed at protecting health care workers from becoming TB-infected on the job is expected to make print by the end of the first week in January.

Onlookers holding their breaths might have been forgiven for comparing the wait on the IOM report to a certain other process holding the nation's attention last month.

"The IOM report will be sort of like the impact of the Supreme Court of Florida's decision on the presidential election," says **Ed Nardell**, MD, chief of pulmonary medicine at the Cambridge (MA) Hospital and TB control officer for the Massachusetts Department of Health. By that, Nardell means that if the IOM comes down hard against new federal regulations, it'll be tough for the Occupational Safety and Health Administration (OSHA) to keep pressing its case for passage of the new rules.

Tantalizing hints suggest that's not about to happen, however, and that the IOM report, like the popular vote, will probably reflect a broad consensus — suggesting that neither the pro- nor the anti-OSHA forces had succeeded in winning committee members over to their respective viewpoints.

Besides, coming down for or against the proposed OSHA regulations wasn't really the IOM committee's charge, says **Marilyn Field**, the health policy expert at the IOM who acted as project officer for the IOM report. "We weren't asked to make recommendations, but rather to try to answer three questions," she says. Those questions were:

— What are the occupational risks of TB?

— How closely are employers already following the 1994 Centers for Disease Control and Prevention guidelines?

In This Issue **continued from page 1**

COMING IN FUTURE ISSUES

- What's up at Ten Against TB?
- New diagnostic tools are coming
- Tracking source cases for kids
- New guidelines for health care workers

— What are the likely effects of passage of the proposed new OSHA regulations?

"The fact that we weren't really asked to address the question of whether the OSHA rules would be good or bad frustrated some on the committee at times, I think," says Field. "As you know, the evidence base is limited and mixed for a number of these questions. That made it hard to do traditional scientific research."

Besides, drawing such sweeping conclusions would take lots of time and money, two resources allotted to the committee in only modest portions, Field adds. "This was, in fact, a short-term project on a small budget," she points out.

The IOM committee met just three times, in April, August, and September. After the third meeting, the committee went to work and wrote its report, which by last month was out the door and off to a three-layer process of review.

First, Field says, a set of experts subjected the report to a peer-style review. Next, a coordinator was charged with sifting through reviewers' comments and passing on final changes in the text suggested by reviewer comments. Finally, the edited report was due to be sent off to a National Academy of Sciences-appointed monitor, whose job was to make sure the reviewers had done their jobs properly.

All that was expected to take time; with Christmas holidays looming, Field was guessing last month that final publication of the report would likely be delayed until at least Jan. 10, more than a week past the originally scheduled end-of-year deadline.

The report will reflect a "considerable amount of consensus," says Field. "The aim is to reach a consensus, but not just to arrive at the lowest common denominator of agreement," she notes. "I think we've done that." Enough agreement was reached that no committee members felt the need to insert signed dissenting opinions, as they might have done, and everyone emerged feeling satisfied their point of view had been presented satisfactorily.

The report is expected to run seven chapters long, counting background papers presented in draft form at the three meetings. In length, it should about equal last year's IOM report on TB (titled "Ending Neglect").

At the OSHA offices in Washington, DC, project officer **Mandy Edens**, MPH, was sanguine as the last days of the year ticked by. "I guess if the report concludes that there's no TB in the United States, and thus no need for an OSHA standard,

we'd have to pull back and reconsider," she says. "But if you read the other IOM report on TB, it says plainly that now is not the time to stop worrying about TB."

Edens was equally unflappable about the prospect of an anti-regulatory Republican moving into the White House. "We've had stuff passed under other Republican administrations," she says. ■

Surprise ouster of Kochi marks passage of an era

Struggle to keep control finally fails

Arata Kochi, the brilliant and temperamental maestro who orchestrated a global revolution in TB control, has been deposed as the head of STOP-TB, landing in a new post (reportedly created just for him) — that of director of HIV / AIDS Care and Support, the World Health Organization (WHO) announced last month.

Kochi's ouster came on the heels of a fierce fight for control of STOP-TB's proposed global drug facility. The surprise move seemed to signal WHO's unwillingness to alienate potential new allies in the expanded fight against TB, as well as a recognition that Kochi's strengths had become, at least for the moment, potentially fatal liabilities.

The former head of the WHO's prestigious Global TB Programme, Kochi had already angered many in the TB community by insisting that STOP-TB — a new WHO division aimed at expanding and increasing partnerships to fight the disease — must be controlled solely by WHO, not by a coalition effort.

This fall, Kochi made a similar bid for control of the proposed global drug facility, a strategy for raising money to ensure a steady supply of good-quality anti-TB drugs to developing nations.

The creation of the drug facility was to have been the topic for discussion at a meeting called by the Rockefeller Foundation, which, along with many other stakeholders, had grown restless with delays by STOP-TB — reputed to be consumed with internal politics aimed at consolidating its own power — in getting the facility off the ground.

Just the day before the Rockefeller meeting was scheduled to take place, Kochi shocked Rockefeller scientific adviser Ariel Pablos-Mendez and others by getting his boss, Director-General Gro Brundtland, to pull out of the meeting. Brundtland's no-show struck many TB experts in the U.S. as bad manners and reportedly left Rockefeller higher-ups steaming. Kochi's removal followed close on the heels of a subsequent WHO pow-wow in Cairo, where Kochi's strong-arm tactics were the topic of many a huddled conversation, and urgent talk of "the need to be more collegial" dominated formal discussion groups.

With Kochi gone, TB experts in the U.S. seem both relieved and sorrowful. "Arata was and is a powerful and charismatic person, " says **Jim Kim**, MD, PhD, executive director of Partners in Health in Boston. "Even though the same qualities that helped him push forward the concept of DOTS are now seen as unhelpful, we'll lose something with his departure. I think we all agree that the TB community owes him an enormous debt of gratitude."

Kochi always thought "outside the box," Kim adds. His ability to do so helped enable him build a powerhouse organization from the flimsy structure he inherited when he first took over the WHO Global TB Programme.

Kochi began the remake of the program by putting together an unorthodox team, consisting of a nimble and affable publicist, Kraig Klaudt, and a streetwise economist recruited from the World Bank, Richard Bumgarner. Bumgarner and Kochi were, from the beginning, a seemingly unbeatable pair, with Bumgarner acting as designated "good cop," smoothing feathers ruffled by Kochi's imperious demeanor.

Almost until the end, Bumgarner stood loyally by his boss, sometimes accused of low-balling cost estimates for DOTS and overstating DOTS' ability to slash TB mortality — and thereby telling financial honchos at the World Bank exactly what they wanted to hear, which ensured the successful sale of the fledgling strategy.

It was a hunker-down, take-no-prisoners formula that meshed perfectly with the perilous times.

Even after Harvard economist Jeffrey Sachs and others began arguing that cheap interventions against "diseases of the poor" might not suffice (and might be, to boot, morally repugnant in a world awash in venture capital and excess cash), Kochi proved willing to think outside the box. As evidence mounted that HIV and multidrug-resistant TB were taking a toll that didn't fit neatly into a DOTS-mediated quick fix, Kochi

risked the wrath of his colleagues by being the first at WHO to swing over in favor of DOTS-Plus. "Let a thousand flowers bloom," he would urge, clipping his L's into R's in his characteristic, rapid-fire fashion.

Jacob Kumaresan was appointed interim head of STOP-TB after Kochi's departure. Along with Ian Smith, former WHO representative in Nepal, Kumaresan is expected to win high marks for the "collegiality" his former boss may have lacking, say observers. "Jacob and Ian are among the most respected and admired people in the TB world," says Kim. "I think people will fall in step right behind them."

As to what the future holds for Kochi, Kim says he envisions a rebirth. "If he gets the same level of financial backing for HIV Care and Support as he did for the WHO TB program, I think we can look forward to something quite amazing happening in that field," he says. With talk afoot of applying the Green Light Committee concept to HIV drugs as well, Kim adds that he looks forward to seeing his old friend across the table again soon.

"I would never, ever count Arata out," Kim says. "I think he'll probably re-emerge, like the phoenix. He may wind up playing an even more prominent role in HIV than he did in TB. I look forward to working with him." ■

UV lights to the rescue in problem-ridden jail

TVA foots the bill for installing new system

No one disputes that the Memphis/Shelby County (TN) jail has more than its share of problems, including overcrowding, high staff turnover, screening procedures that until recently were full of gaping holes, and TB rates that have recently soared to as high as 250/100,000.

All of that makes one recent development at the jail especially welcome. In what county authorities say is a first for U.S. jails, ultraviolet germicidal irradiation has been installed in all six of the jail's air-handling units — and for free, thanks to a grant from the Tennessee Valley Authority (TVA)n working together with the city utility company.

"You don't normally think of a power company trying to stamp out TB, and we're very grateful to them," says **Francis Fountain**, MD, medical adviser to the Shelby County TB control program.

The UV fixtures have been installed inside the jail's ventilation system, and not as free-standing fixtures, adds Fountain. Their manufacturer claims they'll kill 99.9% of airborne pathogens, TB included. The one place the lights haven't been installed is inside the jail's medical facility, where air is exhausted directly to the outside, Fountain adds.

The decision to install UV lights — as opposed to, say, purchasing a digital chest X-ray unit — was based partly on the need not to add any new steps to the intake process, says **Vincent Glover**, manager of the county health department's infectious disease program. "They process someone through the intake facility once every seven minutes, and they contend that adding anything at all to the process that make it longer is simply not acceptable," Glover adds.

The jail is the fifth-largest in the country. With a daily census that stands at about 2,800 people, it's operating at almost twice its capacity of 1,600 people. The Criminal Justice Center, the intake point for the system, is supposed to feed inmates into other county-run facilities after 10 days, Fountain explains. Inmates who are sentenced to more than a year are supposed to be shipped off to the prison system. In reality, the intake facility acts as a bottleneck, meaning the jail functions as a de facto prison system.

To make things worse, the county mental health facility has only 125 beds, says Glover. That means the jail also acts as a holding tank for mentally ill homeless residents of the city. At any given point in time, he estimates, there are upwards of 500 mentally ill inmates housed in the jail.

All these problems must be managed on a meager budget of $2.5 million in funds from the county, Glover adds. The result is high turnover among the jail staff, a fact Glover says is hardly surprising. "The jail administration doesn't want to take TB home to their families," he notes. "As I see it, the biggest problem is the lack of funding made available to the jail."

Along with engineering the collaboration with TVA that brought in the UV fixtures, TB controllers have been hard at work overhauling screening procedures at the jail, says Glover. From skin-testing just 200 people a year, the jail

is now up to testing 5,000 a year, with male inmates having to wait no more than 10 days for a TB test, Glover says.

At the women's jail, new screening policies are about to go into effect that will skin-test female inmates as soon as they hit the door. Along with mandatory TB testing, HIV and syphilis testing are being offered at the same time, and syphilis case-finding is up substantially as a result, says Glover.

"As I look back over the last two years, I can see considerable changes," Glover says. One of the most promising changes is the construction of a new intake facility, now under way. "That should reduce some of the chaos and the backlog," Glover notes. "Maybe eventually it will give us the chance to do screening on intake" at the men's jail as well, he adds. ■

New vaccine candidate uses modified form of BCG

Old vaccine retooled to overexpress large protein

A new TB vaccine candidate using a genetically modified version of the BCG vaccine has so far delivered promising results in guinea pigs challenged with TB, says its inventor, **Marcus Horwitz**, PhD, professor of medicine in the department of medicine and microbiology, immunology, and molecular genetics at the University of California in Los Angeles. The vaccine is expected to enter human safety trials within the year, he adds.

Horwitz says he modified the BCG vaccine to make it over-express one of the proteins secreted by the TB mycobacterium. That protein, Antigen 85-B, is used to build the bug's cell wall. Because it is the most abundant protein, Antigen 85 seemed from the start a likely candidate for triggering an immune response, says Horwitz. Because it is secreted outside the mycobacterium, it is readily available to the immune system for recognition and processing.

"We'd already done some work that showed extracellular proteins are important immunoprotective molecules for intracellular parasites in general," say Horwitz. "In addition, we'd shown that purified extracellular proteins induced protection. We decided to focus on the 30 KD protein, the Antigen 85 protein, because it's the most abundant secretory protein."

In fact, when Horwitz immunized guinea pigs using just the Antigen 85 protein in combination with an adjuvant, results were good, he says. The problem was that the immune response wasn't as strong as he'd have liked.

Trial and error suggested that BCG might make a better delivery vehicle than the adjuvant. BCG met the qualifications on several counts, he explains: "We needed a host that wasn't pathogenic, but that would reproduce readily," he says. In some respects, E. coli might have been a candidate, because it, too, produces the Antigen 85 protein, albeit in small quantities. *M. smegmatis*, on the other hand, secretes the protein abundantly, but doesn't multiply readily in the host.

Perhaps BCG's biggest plus is that it not only reproduces briskly, churning out sufficient quantities of Antigen 85 as it goes along, but also encodes the protein in its native form — that is, folded in the same way as if *M. tuberculosis* were making it, says Horwitz.

Once he'd settled on BCG as the host, experiments showed that Horwitz's genetically tweaked version of the century-old vaccine gave a lot better protection than did ordinary BCG.

For now, Horwitz says he's working on ways to increase the potency of his candidate vaccine, perhaps by lengthening the interval between immunization and challenge. In a preliminary experiment when he did just that, the test animals did indeed show more protection, he says. ■

Spat over pocket cards pits state against state

Binational cases caught in a tug of war

A wallet-sized pocket card is at the center of a squabble between groups in Texas and California. The trouble centers around which of two groups — CURE-TB, based in the San Diego department of health, or the Texas organization known as TB NET — gets what might be called referral rights to binational TB cases.

The Centers for Disease Control and Prevention (CDC) in Atlanta, trying gamely to broker a solution between the two camps, has suggested piloting a third, wallet-sized card that will be

piloted in Texas, California, and some third inland location.

But what exactly the third card will say or do isn't yet clear. The hope seems to be that its creation will give everyone in the fight a bit of breathing room, allowing the disputants to step back and try once more to work out their differences.

Both groups consist essentially of data banks and referral services, amounting to, in the case of TB NET, a toll-free number and a pocket-sized written patient record, and in the case of CURE-TB, simply a wallet-sized card that features a toll-free number. Both groups were created to accomplish the same purpose: ensure continuity of treatment among binationals.

There's nothing especially remarkable about the overlap. After all, tons of competing groups have traditionally proliferated along the U.S./Mexican border, all jockeying for funds, attention, and space. What lends urgency to the situation is that when active cases among binationals do turn up, the Mexican government (along with other interested parties) needs to know which of the two groups to call.

"The Mexicans don't know the difference between CURE-TB and TB NET," points out **Kayla Laserson**, epidemiologist at the Division of TB Elimination at the CDC. "They just know that there needs to be more cross-referral between the two groups. So we're trying to get them to sit down and come to some formal agreement."

Division of labor could be possible

One tentative solution that seems to be shaping up is a division of labor whereby TB NET handles latent infections and CURE-TB takes charge of active cases. The rationale for that division goes something like this:

Both groups handle tracking and referral for active cases and latent infection. But TB NET, with its flip-out paper record of patient care, was designed to serve the needs of providers who care for migrant workers who are moving from state to state, not back and forth across national borders. So TB NET, it's reasoned, is best equipped to handle tracking patients who move within the United States.

CURE-TB, with just a toll-free number (and no telltale paper record that might cause problems for someone trying to cross a national border), should by the same logic take charge of keeping track of active cases moving across the U.S./Mexican border. Because Mexico's priority is treating active cases, not latent infection, the proposed solution takes it one step further: Why not let CURE-TB take care of active cases, while TB NET looks after latent infections?

On the face of it, that sounds simple. In fact, this is where things begin to get sticky. For one thing, both groups have been tracking both active cases and contacts, and neither is eager to let go of either group, says **Charles Wallace**, chief of TB control in the state of Texas.

Plus, to TB NET — which originated the idea of a portable pocket-sized record and toll-free number five years ago - CURE-TB feels like an interloper that came along and stole the idea of a pocket card.

"Both programs perform essentially the same functions, even though CURE TB has only recently become interested in tracking contacts as well as cases," Wallace says. "The real difference, as I see it, is that one program, CURE-TB, is part of the existing health department infrastructure. The other, TB NET, operates out of a community-based organization, the Migrant Clinicians' Network." Like water and oil, the two infrastructures have little affinity for each other, a fact that's only exacerbated the politics of the dispute, as Wallace sees it.

There are logistical issues as well, says **Del Garcia**, spokeswoman for the Migrant Clinicians' Network, which in turn is both the founder of TB NET and the name of the 1,700-member organization of providers who work in migrant health centers. For one thing, Garcia says, the decision to delegate active cases to CURE-TB overlooks the fact that in some far-flung Mexican locations, phones aren't available, meaning that a paper-free referral system depending solely on a toll-free number simply won't work.

"You have health units out in the middle of nowhere where they're functioning with a CB radio, and a phone or fax machine simply aren't resources that are available," she says. "But I'm not sure everyone [in the dispute] understands that."

Additionally, Garcia says, it makes no sense to ask TB NET to refer all its active cases out of the community-based organization infrastructure into the health department infrastructure. One problem is that in some places the two systems sometimes consist of the same lone physician. "In some places, the doctor who works in the migrant clinic is also the doctor who serves in the health department, so you're basically asking him to refer from himself to himself," she says.

The other problem is that in many far-flung rural outposts in America, migrants may have no easy access to a health department. "If you're a migrant worker in Chicago or Los Angeles, that's one thing; there, of course, we'll gladly refer active cases to the local health department. But in Arcadia, WI, or Chambersburg, PA, the health department may only be open three days a week. There may be only one nurse who divides her time between diabetes, maternal and infant health, and TB. And that one nurse probably doesn't speak Spanish."

As Wallace points out, with four or five migrant streams and a 2,000-mile border, there ought to be enough work to keep everyone busy and happy. "There's enough to go around for everyone," he says. "It would unfortunate if in the end we can't get these two agencies to sit down and agree." ■

TB Monitor *interview*

TB drug market 'poorly understood by industry'

TB to enter '3rd Revolution,' says Roscigno

Giorgio Roscigno, MD, is the new CEO of the newly created Global Alliance for TB Drug Development. His resume includes wide-ranging experience in both public health and private industry; his reputation is that of someone who has functioned as a conscience for the drug industry, continually encouraging it to do better by the poor.

Certainly, the facts bear that role out. On the (very) short list that might be called "Big Pharma's Contributions to Tropical Medicine," thanks are owed chiefly to the U.S. military for developing three anti-malarial compounds; the veterinary industry, which invented six more drugs that have proven useful in humans; and to Roscigno, who oversaw the development of eflornithine, a drug used to treat African trypanosomiasis (sleeping sickness), and rifapentine, the only new compound developed for TB treatment in the past 25 years.

Says **Ariel Pablos-Mendez**, MD, scientific director of the Rockefeller Foundation: "You can see why we think we have gotten the right man for the job."

Following are excerpts from a *TB Monitor* interview with Roscigno:

Q: How did you become interested in public health?

Roscigno: I am an Italian born in Eritrea, the breakaway part of Ethiopia. My mother's family emigrated there the end of the last century; it was there my elder daughter was born. I worked in Ethiopia, Sudan, Nigeria, and Zaire, and that's how I came to have a passion for public health and tropical diseases. [Editor's note: After a two-year stint in private practice in Italy, Roscigno joined one of the precursors to Aventis, where he survived a steady succession of mergers, and where he served first as medical director in both Africa and in Asia, and later as director of clinical research in Europe.]

I always hoped my work in private industry would bring me back to my original interests, and in that way, I've been quite lucky. Being in charge of eflornithine development, being on the decision team with rifapentine — these things are like children to me in that I've always hoped they would mean more than just commercial success.

Q: Some people say Big Pharma has seriously underestimated the potential of the TB drug market; others say that given their shareholders' priorities, the drug industry can never be persuaded to gamble on drugs tailored to meet the needs of people living in poor countries. What do you think?

Roscigno: Certainly the TB drug market is poorly understood by industry. Small- and medium-scale industry are often unaware of potential markets, and big industry is reluctant to believe they will ever make any return on investments. That's why the Alliance is preparing a report which will discuss the scope of this market, its nuances, its size, and how to segment and access it.

At about $500 million to $600 million, this market is quite substantial; the tricky part is that it's widely spread throughout many countries, and a lot of it's in the public sector, so it is not easy to access. And despite the fact that current TB research is very active, both in academia and in the public sector, industry often fails to pick up many good ideas and leads. So there is this gap, this void that needs to be filled.

We can fill that gap first by elucidating the market size, and so creating some interest; and second, by establishing an alliance of partners and stakeholders, which can help move some of these products from early discovery to development.

Q: Besides the market report, what other activities are already under way at the Global Alliance?

Roscigno: As you know, 25 scientists from all over the world have contributed to the Alliance's Scientific Blueprint [for new drug development], a state-of-the-art document full of insights that should prove valuable to anyone interested in the current research on TB. We've also put out a call for proposals, and we expect the first round to come in by Dec. 15. In addition, we're proactively going out and provoking discussions about development of various promising compounds — carrying on both active and passive case-finding, you could say.

Q: You say that by 2010 the Global Alliance will have produced a new TB drug that will shorten therapy to two to three months. You also say that such a discovery will amount to a "third revolution" in TB control, equal in importance to the development of short-course therapy and the DOTS strategy. Where in current research activities do you believe that new drug is most likely to emerge?

Roscigno: Although we still have no drug in therapeutics that has gone the genomic route and made it onto the market, I have very strong faith in genomic research. So does most of Big Pharma, which is why they're investing heavily right now in genomics. Theoretically, the genomic route is the easiest way to go. For example, the discovery of the gene that induces latency would bring us very close indeed to our goal of a drug that works in just two or three months. Still, I would never rule out exploring other uses for existing drugs.

One other thing the Alliance is working on is how to shorten the period of time needed to register a drug — the clinical trials, the years spent waiting for relapses — which is now quite a long and tedious exercise. That's why we're encouraging activities aimed at finding some sort of surrogate marker that can be used to predict relapse rates. ■

WHO pulls out of meeting at last minute

Does drug facility squabble reflect power grab?

STOP-TB's global drug facility, a good idea that's been trying to get off the ground for the last couple of years, was the focus of a spat last month between TB experts at the World Health Organization and a "working group" impatient to get the facility up and running.

The idea behind the global drug facility is basically a simple one: to collect a pot of money from various donors and stakeholders and use it to help national programs get through temporary shortfalls that threaten to interrupt the steady flow of TB drugs.

The drug facility, an idea that's been on the drawing boards for upwards of two years, was supposed to have been run out of the STOP-TB division of WHO. The problem, some say, is that STOP-TB has been too consumed with its own internal politics to devote any attention to getting the drug facility up and running.

Having jump-started the Global Alliance for TB Drug Development, the Rockefeller Foundation decided to call a working group of "interested stakeholders" (including, of course, reps from STOP TB) to get the ball rolling. Once the working group was established, the pace of events quickened. At the working group's initial meeting back in July, a second get-together had been scheduled to take place in New York early last month. There, the idea was to draw up a charter, which would be presented at a subsequent meeting in Bellagio, Italy, when WHO would officially announce the formal creation of the drug facility.

An e-mail arrives: 'We won't be there'

But at the last minute, WHO Director-General Gro Harlem Brundtland dispatched an e-mail to Rockefeller announcing that her organization was pulling out of the New York meeting. TB experts on this side of the Atlantic began to fret about whether that signaled a power struggle that might jeopardize the drug facility's future.

"If STOP-TB tries to get hold of it, there may be a problem," says **Lee Reichman**, MD, MPH, director of the National TB Center at the New Jersey Medical School in Newark. "They've done this kind of thing before. STOP-TB used to be a partnership, and then WHO said no, they had to be the leaders. It could happen again."

At Rockefeller, the tone was more conciliatory. "In my mind, we are partners with STOP-TB, and no one is taking orders from anyone because that's not the issue at hand," says **Ariel Pablos-Mendez**, MD, scientific director of the Rockefeller Foundation. "All that matters to us is that the drug facility will be established."

Back in Geneva, WHO defended its move by saying the working group didn't have "all the stakeholders" at the table, and that it is important to be make sure careful control is exercised over how TB drugs are made available and how they are used.

"You can't just look at one dying patient in East Timor or someplace and decide you have to throw drugs at the problem. That would create a disaster," says **Jacob Kumaresan**, medical officer with STOP-TB. That was just one of the many reasons WHO decided to bail out, he adds.

For one thing, the meeting "was poorly planned," says Kumaresan. "It was organized at the last minute, and there hadn't been any agreement ahead of time about the outcome." Also, high-burden countries weren't adequately represented. "There was only one representative from a donor country . . . who was going to be there," he says. "Many of the potential donors weren't there either. It was simply too far to go for just one meeting."

Private industry vs. public sector

The trouble boils down to the existence of two competing visions for the drug facility, which have yet to be reconciled, he goes on. "One is the perspective of private industry, which is the perspective of Rockefeller. It has its strengths, which include independence, flexibility, and responsiveness."

The other vision, that of a public-sector model, has its strengths, too, he adds, and their omission would be dangerous. As far as donors are concerned, WHO's presence is essential to ensure "credibility," he says. As for the high-burden countries that stand to benefit from the drug facility, only WHO can provide the contacts with technical programs, make sure drug supplies are available "for the long term — at least for the next 10 to 15 years," and keep a tight grip on how the drugs are used. "Otherwise, we'd just create a public-health disaster," he concludes.

By the end of last month, the dust had begun to settle, and conciliatory messages had been exchanged between the two groups. "What matters is that there are good wills around the table, and that things are moving very fast, both on the technical side and on the political side as well," says Pablos-Mendez. "The working group continues to work. And so we are hopeful." ■

TB transmission from a foreign-born child

Source: Curtis AB, et al. **Extensive transmission of Mycobacterium tuberculosis from a child.** *N Engl J Med* 1999; 341:1491-1495.

A 36-year-old woman was found to have tuberculosis (TB) arthritis of one hip joint without pulmonary involvement or infectivity. She had had no known contact with anyone with TB, lived in a part of North Dakota where TB is rare, and had only left North Dakota for a trip to Montana. Evaluating contacts, her 9-year-old child (who had joined the family from the Marshall Islands 2 years earlier) was found to have cavitary pulmonary TB. In retrospect, it was noted that the child sometimes fell asleep at school and had had a "dry cough" for a few months prior to diagnosis. After arriving in North Dakota two years earlier, a TB skin test had been placed but not read.

Careful evaluation suggested that the woman had probably contracted her infection in 1997. Thus, rigorous testing of the child's other contacts was done. Three of four household contacts had positive skin tests (the guardian with TB in the hip and a twin brother with a positive sputum culture), as did 16 of 24 classroom contacts, 10 of 32 school bus riders, and nine of 61 day care contacts. Appropriate treatment was given.

*Comment by **Philip R. Fischer**, MD, DTM&H*

By conventional teaching, young children are not contagious for TB because they rarely generate a forceful enough cough to aerosolize and spread organisms. This child in North Dakota represents an alarming exception to conventional teaching. He not only had cavitary disease before being ill enough to prompt medical evaluation, but he had already spread active disease in his family and TB organisms to 20% of his contacts. Clearly, children in the first decade of life can spread TB.

Published recommendations can guide the evaluation of foreign-born children who are adopted into families in the United States. In

particular, the history of having been vaccinated with BCG vaccine should not affect the decision about whether to place a TB skin test.[1] The source patient in North Dakota had appropriately been subjected to TB skin testing, but the result of the skin test was never noted.

Policies vary for reading TB skin tests. Some health care providers require that results be read by medical personnel 48-72 hours after test placement, and others accept readings by presumably reliable patients or guardians. As sadly illustrated in North Dakota, providers should ensure that TB tests are not only placed but are also read and results documented. To facilitate this, medical offices should implement follow-up systems to confirm that tests are either read or repeated (and then read).

In addition to TB skin testing, what other evaluation should be done for adoptees and other children who are newly arrived in the United States? As reviewed in *Travel Medicine Advisor Update* in 1998, laboratory assessment could include tests for hepatitis B (both antigen and antibody testing), HIV, syphilis, and intestinal parasites.[2] A blood count is also usually advised (with attention to anemia and to red cell indices). Increasingly, hepatitis C testing is also recommended because helpful treatment might be available. Assessments for normal, age-appropriate hearing, vision, dentition, development, and immunizations are also indicated. Though debatable, some experts recommend testing asymptomatic new arrivals for lead toxicity, thyroid dysfunction, and renal disease.

The source patient in North Dakota had his TB test placed "shortly after" arrival in the United States. When should TB testing be done in immigrants and foreign-born adoptees? Because some children coming into the United States could be in a "window" period between infection and conversion to a positive test, individuals testing negative initially could be retested six months later. Similarly, follow-up repeated testing for HIV and hepatitis C could be considered in children who tested negatively on arrival.[3]

The experience reported from North Dakota serves as a poignant reminder of the ability of *M. tuberculosis* to spread subtly through a community. Equally, the case demonstrates the public health implications of a missed screening opportunity. It also reminds us to screen new arrivals in the United States carefully. TB testing should be initiated and completed. Other testing, as adapted to the particular situation, should also be done. Follow-up is critical, and new arrivals must be integrated into the health care system.

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Western blot test may be a better way

Source: Franchi A, Amicosante M, Rovatti E, et al. **Evaluation of a Western blot test as a potential screening tool for occupational exposure to *Mycobacterium tuberculosis* in health care workers.** *J Occup Environ Med* 2000; 42:64-68.

Is there a better way to test health care workers for occupational exposure to TB? Researchers at the University of Modena in Italy say there is: Using a Western blot test to detect an antibody as a marker of exposure to TB.

Currently, skin tests measure the reaction to tuberculin purified protein derivative (PPD) to screen health care workers for risk of TB infection. The researchers developed an *M. bovis* serological Western blot test as an earlier marker of TB contact.

The antibody test could not be used with BCG-vaccinated workers due to their high reactivity. But among non-vaccinated health care workers, the Western blot test did, in fact, detect exposure earlier than the PPD skin test and with greater sensitivity. For example, the Western blot test identified 95% of workers in the TB and respiratory diseases division as being sensitized to *Mycobacterium tuberculosis*, as compared to 73% identified by PPD. In the infectious disease division, Western blot identified 59% of workers as sensitized, compared to 41% identified by PPD.

On the downside, the authors noted that the Western blot methodology "would give more limited information about the level or intensity of MTB-exposure than the PPD skin test.

"Overall, this study suggests that the WB test antibody market, as a sensitive indicator of MTB contact among exposed HCWs, might provide, in association with the PPD skin testing, new tools to assess the TB risk in health care facilities with higher accuracy, thus allowing a more timely and appropriate implementation of the environmental and health surveillance measures for the primary prevention and control of TB infection in the workplace," the authors stated. ▼

Non-employee docs should be immunized and screened

Source: Bratcher DF, Stover BH, Lane NE, and Paul RI. **Compliance with national recommendations for tuberculosis screening and immunization of healthcare workers in a children's hospital.** *Infect Control Hosp Epidemiol* 2000; 21: 338-340.

Hospital-based, non-employee physicians should be included in mandatory immunizations and tuberculosis screening, researchers at Kosair Children's Hospital in Louisville, KY, concluded.

A survey of 55 physicians and 351 hospital employees found different patterns of compliance with national immunization and TB guidelines. Only 40% of physicians reported having an annual TB screening compared to 93% of employees.

"Many states require annual TB screening for health care facility employees, and there are published recommendations and guidelines for TB screening programs to include all health care personnel," the authors note. "Despite these recommendations, physicians have not been included in many hospitals' employee-health programs, and they fail to have annual TB screening."

The disparity was not as great for immunizations, but lack of compliance was still significant. Eighteen percent of physicians and 14% of employees indicated they had incomplete hepatitis B virus status. "One half (5 of 10) of physicians reporting an incomplete HBV vaccine series were specialists who regularly performed invasive procedures," the authors noted.

Most physicians indicated they were aware of the national immunization recommendations for health care workers. Why are there gaps in immunization and screening for TB? A moderate to high factor, according to 94% of physicians, is the lack of mandatory participation in an employee health program. Lack of availability of an employee health program was cited as of moderate to high importance by 74% of the physicians.

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"We recommend that mandatory immunization and TB screening policies encompass all HCWs, including physicians," the authors concluded. "Compliance with these policies may require enforcement through the credentialing process or through other innovative strategies that circumvent time-constraint issues."

Interestingly, the study found one area in which physicians had a significantly higher rate of immunization than hospital staff: influenza. Some 57% of physicians reported having an influenza immunization, compared to 31% of employees. The authors noted that both rates are "alarmingly low," and speculated that the higher rate among physicians may be due to greater awareness of recommendations or less concern about potential side effects or complications from the vaccine. ▼

Ouch! Penile tuberculosis from BCG vaccine

Source: Latini JM, et al. *J Urol* 2000; 163:1870.

An unfortunate elderly man with transitional cell carcinoma of the bladder developed progressive dorsal penile nodules and a coronal abscess two weeks after completion of a six-week course of weekly intravesicular bacillus Calmette-Guerin (BCG) (a live attenuated strain of *Mycobacterium bovis*).

The BCG treatment had been uneventful except for transient dysuria following the final installation. The coronal abscess did not respond to incision and drainage or antibiotics. An excisional biopsy was performed, which revealed non-caseating granulomata and fibrous tissue. Cultures for HSV, bacteria, and fungi were negative and AFB smears were negative. Eventually, *M. bovis* grew from culture, and the lesions quickly responded to antituberculous therapy.

Interestingly, the man had contracted pulmonary tuberculosis in 1955 in Korea, requiring segmental lobe resection and nine months of treatment with isoniazid and p-aminosalicylic acid.

Urethral and penile complications from intravesicular BCG are rare but should be suspected in patients with evidence of penile induration or infection in whom routine cultures are negative, irrespective of the results of AFB smears. Current recommendations support the use of PCR in such cases, which may have resulted in a speedier diagnosis. ■

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. ■