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Quantiferon guidelines call for using TST as a back-up test

But only to check positive results

New guidelines for Quantiferon, the newly approved diagnostic test for latent TB infection, will probably suggest using the tuberculin skin test (TST) to confirm positive Quantiferon results.

"In essence, we'll use Quantiferon as a screening test for the TST, at least for now," says **Gerald Mazurek**, MD, the epidemiologist at the Centers for Disease Control and Prevention's Division of Tuberculosis Elimination (DTBE) who has overseen years of trials of the new diagnostic aid in the United States. Using a TST to confirm positive results won't drive up costs appreciably, because most tests will be negative anyway, Mazurek adds.

The decision to retain the skin test as a backup is mostly aimed at raising users' comfort level, Mazurek adds. But it's also an acknowledgement that no one has ever followed subjects who tested positive to see what happens.

"There's simply not a big cohort of people who've been tested and followed through their lifetimes," says **Elsa Villarino**, MD, MPH, chief of the therapeutics and diagnostics section at the DTBE. "Nor will there be, since if you consider someone infected, you're obliged to treat them."

Still, that doesn't mean the new test isn't trustworthy, say Villarino and Mazurek. Autopsy studies of cattle tested with Quantiferon provide a gold standard the TST is lacking and confirm a tight correlation between Quantiferon results and the presence of TB infection.

"Personally, I'm more comfortable with Quantiferon than the tuberculin skin test, and I think that based on the data, it's a more sensitive test and a better test," says Mazurek. "But the world doesn't have that much experience with Quantiferon, so I think it's reasonable

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for our first step to be a small one."

If the test performs as expected, revised guidelines that would recommend dropping the TST and using Quantiferon results as the sole basis for deciding whether to offer treatment for latent TB infection might be issued at some point, Mazurek adds. The first set of Quantiferon guidelines should be out sometime later this summer and will be included in a *Morbidity & Mortality Weekly Report* article that will also address issues related to skin-testing.

Two risk categories, two cut-points

The guidelines are expected to lay out two broad categories of risk — "low" and "other" — with a different cut-point assigned to each. With Quantiferon, the two cut-points will correspond not to millimeters of induration, as with the TST, but to two percentages of "optical density," which indicate the percentage in a blood sample of lymphocytes that are sensitized to test antigens.

Thus, a blood sample sensitized to the tuberculin purified protein derivative (PPD) antigen will produce between 15% and 30% more gamma interferon than the mitogen, the test's control antigen. Subjects judged to be "low risk" must score at least 30% before they can be considered positive; those in the other, higher-risk category need score only 15%. Results can be read visually, but the test also comes with computer software to interpret results, Mazurek notes.

Unlike the tuberculin skin-test, there's nothing subjective about the test's reading, says Villarino. What is subjective, however, is the determination of the risk category in which to place a subject. In some instances — health care workers come to mind — there is an ongoing debate about how to make the decision, she concedes. "To me, that's not an issue," she adds. "I say, look at who the health care worker is and what they've been doing."

The draft guidelines were scheduled to be presented before audiences at the American Thoracic Society's annual meeting in Atlanta in May, and also at the National TB Controllers Association meeting in June. "We don't expect to get more data; we simply want to formally solicit their input," says Villarino.

The test was originally developed by an Australian veterinarian to detect TB in cattle. It measures the level of gamma interferon (INF-G) produced by lymphocytes sensitized to a specific antigen. The test contains normal saline, used as

a negative control; a mitogen, used as a positive control; tuberculin PPD; and *Mycobacterium avium* PPD. Lymphocytes in blood samples produce INF-G in proportion to the degree to which they have been sensitized. Thus, the test can distinguish whether someone has been sensitized to TB or to *M. avium*, an atypical mycobacterium that may cause a cross-reaction with the TST.

Because the test uses a one-step blood draw, it doesn't require subjects to return two to three days later for a reading, as does the TST.

Quantiferon was approved recently by the Food and Drug Administration for use in the United States. ■

Food-service industry focus of Denver debate

Should license be linked to PPD?

Some TB experts in Denver want to implement a program of mandatory TB screening that targets foreign-born workers in the food-service industry by making them complete a skin test before they go to work.

If that sounds a bit draconian, consider the experts' reasoning: TB cases in Denver are up from 63 cases in 2000 to 91 cases last year, with most of the increase among the foreign-born. In Denver, as elsewhere in the country, many of the food-service workers who staff the kitchens of the city's restaurant industry are foreign-born, and many are medically underserved, local TB experts say. Federal guidelines, in fact, single out food-service workers, saying that group may be an occupational sector where TB screening is important.[1]

Until a few years ago, Denver did have such a program. In its final version, the program was set up so that only high-risk workers were pulled for TB testing. Latency rates among that selected subpopulation were over 30% tuberculin skin-test positive, showing that the program was needed, its boosters say. More important, they add, the program snagged a handful of active cases among food-service workers that otherwise may have gone undetected for much longer.[2]

"With a rising incidence of TB in Colorado, anything you can do to identify those at high risk for TB is something you should do," says **John Sbarbaro**, MD, professor of medicine at the University of Colorado Health Sciences Center in Denver. Sure, Sbarbaro adds, there are high concentrations of foreign-born workers in other industries as well, such as migrant farm workers, roofers, and landscapers, but they're simply not as accessible.

"It would great to screen migrant farm workers too, but there's no central place to do it," he argues. "Here in metro Denver, the TB clinic is right in the middle of town, a bus ride away from most restaurants. You get your card, and away you go."

Once upon a time, a great program

It was Sbarbaro, in fact, who inaugurated the original screening program in the early 1970's when he served as Denver's director of public health. During its genesis, the program screened as many as 12,000 food-service workers a year. Over the years, however, it became clear that most of the pertinent epidemiology was increasingly concentrated among foreign-born workers, so the program was refined by inserting a questionnaire that flagged applicants if they met any of several high-risk categories.

That whittled the pool of people who had to be skin-tested down to only about 2,500 food-service applicants a year, the vast majority of whom were foreign-born, and about one-third of whom turned out to be skin-test positive.

Then — for reasons that Sbarbaro and others assert have more to do with politics than good policy — the program was shut down.

It's important to know that one reason the original program functioned so smoothly was because workers already had to trek to the health department to take a food-handler test. That involved watching a movie about food handling and taking a test on the contents. Because job applicants already had to make the trip to see the movie, it wasn't much trouble to require them to take a TB skin test while they were there.

But at a certain point, the food handler test requirement was dropped. Then the restaurant trade association claimed that forcing food-service workers to make a trip to the health department solely for a TB skin test was an inconvenience. Further, they argued that it was unfair because they were the only industry in town so burdened.

At that point, according to one version of the story, the situation became politicized. First, the regulatory and enforcement arm of the city's public health department was severed from the medical

State TB law makeover in works for Colorado

MDR patients must finish treatment

At press time, Colorado was a breath away from getting a new TB statute, one that would allow TB controllers to confine non-adherent patients with multidrug-resistant (MDR) TB until they have finished their course of treatment.

The old statute, which was last updated in 1960, specifies that recalcitrant patients can be confined only until they're rendered "noninfectious." The new law would extend the reach of the statute in the most logical of ways, its supporters say, as well as take aim at patients with the most dangerous kind of disease.

The trouble with the wording of the original law, crafted back when what it meant to be "infectious" wasn't as clearly understood, is that lawyers often interpret it to mean "no longer actively infectious," notes **John Sbarbaro**, MD, professor of medicine at the University of Colorado Health Sciences Center in Denver. "But even if you no longer have a [sputum-smear] positive culture, you can still reactivate," he adds. "If you're going to protect the community, you've got to do it based on the reality of pathogenesis."

Hedging bets by not asking too much

It would have been useful to extend the state's power to hold all non-adherent patients, drug-sensitive ones included, until they had finished treatment, says **Ned Calonge**, MD, the TB program's medical director. "But we worried that that would jeopardize passage of the new statute, and we wouldn't get what we wanted the most, which was the ability to hold those with MDR-TB." The new statute also codifies the state's ability to conduct contact investigations, he adds.

All signs pointed to the new statute being approved and enacted. By last month, the bill had cleared three readings in the legislature and awaited only a signature from the governor. ■

arm as the unintended consequence of a procedure aimed at giving more financial security to the city's indigent care hospital.

With little public health expertise, this side of the story goes, the then-director of the agency where enforcement power now resided — by that time re-christened the Board of Environmental Health — caved in to pressure from the food-service industry.

At the meeting where it was decided to shut down the program, public health experts weren't even invited to speak, says **Frank Judson**, MD, director of the Denver Department of Public Health. "We went on our own, but my testimony was interrupted after only two minutes," recalls Judson.

That's not what happened at all, retorts **Bob Conrad**, acting manager of the Board of Environmental Health. Conrad, who was not in office at the time the screening program was axed, says the city's lawyers had strong misgivings about a program that singled out one industry. "There was pressure from the restaurant association, but that had nothing to do with our decision," Conrad says. "Few, if any, health departments around the country do such focused screening. I'm not a doctor, and I'm no expert, but why single out TB? Why not hepatitis or another communicable disease?"

Ned Calonge, MD, Colorado's chief medical officer (and not a member of Conrad's department), sides with Conrad. It wasn't fair to make only food-service workers come to the health department, Calonge says. "They didn't single out other industries where the foreign-born worked, so the effect was to place differential pressure on the food-service industry," he says. Far more important, to Calonge's thinking, is getting the governor's signature on a bill that would update the state's TB statute. **(For more information on the statute, see story, above.)**

But to Judson, the program didn't "discriminate" against the food-service industry; it provided an important service (albeit one the food workers didn't have the right to turn down) that certain other industries should be getting as well.

"The fact that you can't reach everyone who'd benefit from screening — the roofers, the construction workers, the cab drivers — is not a good reason not to do something," Judson says. Programs that targeted other industries where foreign-born workers are also concentrated simply wouldn't be

feasible, he adds. "I don't know who's out there doing weekend roofing, or running an unregistered lawn and garden service," he points out. "We have no way to reach these other industries."

Nor does it trouble Judson that no other jurisdiction in the country, evidently, has a program targeting food-service workers. "The mere fact that you're creative and innovative enough to come up with a program others haven't done yet is a good reason to do this," he says. Las Vegas actually had such a program until recently, but with fewer foreign-born workers than Denver, the program was eventually cancelled because it was deemed to be too low-yield to justify its continued existence.

Whatever its merits, almost everyone in Denver agrees the prospects for starting the program back up are not especially promising. "It would be harder to do, since we no longer have the food-handler test," says **Randall Reves**, MD, medical director of the city's TB control program. More likely, there will be some sort of move to start voluntary outreach programs, he adds. That means finding money, of course, and the state of Colorado doesn't provide money for targeted testing.

Looking at cabbies and bus drivers

At the same time, Reves concedes he's intrigued by the prospect of using a licensing procedure to access particular industries dominated by foreign-born workers. Last year, for example, three active cases of TB were reported among taxi and bus drivers, a number that suggests the case rate is even higher among cabbies and bus drivers than in the food-service industry, because it's a smaller job sector. As it happens, there's already a licensing procedure in place for cabbies and bus drivers, so in that industry, a mandatory screening program "might actually make sense," he says.

What Reves seems to hanker for most, though, is a sort of paradigm shift. "To me, the question is whether people should be thinking about TB risk assessment as a part of pre-employment screening," he says. "The point is to find ways to do it that are effective but impose the least aggravation."

After all, he says, no one disputes the requirement that children starting school have to provide proof they've gotten their immunizations. "It doesn't really make sense for kids to wait until they hit the first grade to get immunized," he adds. "It's just that first grade is a logical place to do it, since that's where everybody goes."

Some employment sectors such as the meat processing industry have been hard-hit by TB outbreaks and have reacted by implementing TB screening for job applicants. By inserting a simple risk assessment for TB into the application process, just like the food-handlers' test was doing before it was scrapped, employers could easily spot candidates for TB skin testing and offer the test when indicated.

References

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AIDS fund awards get off to bumpy start

Crucial step, but long way to go

The first round of awards by the Global Fund to Fight AIDS, TB and Malaria was marked by a flurry of publicity, some accolades, some complaints — and calls for much more money, much faster.

Harvard economist **Jeff Sachs** compared the April 29th awards to "the first moon launch," while **Jim Kim**, MD, PhD, executive director of Cambridge, MA-based Partners in Health, dubbed it "a Rosa Parks moment," referring to the civil rights-era figure who galvanized a successful strike against a public transportation system.

Yet several groups charged that the fund's original intent — to get treatment to AIDS victims — was intentionally subverted, in part because rich countries pressured poor ones to scale back requests for costly treatment programs. "Only six applications had substantial treatment components for people with AIDS," says **Paul Davis** of ACT-UP, the Philadelphia-based AIDS activist group that has helped move the global AIDS treatment issue to the forefront of the political agenda. "One reason was because bilateral donors put the

thumbscrews to developing countries, forcing them to ratchet down the size of requests," he adds.

At the New York offices of Medecins Sans Frontieres, spokeswoman **Chris Torgeson** agrees with Davis: "That did happen," she says. "People close to the selection process know that it did."

A doomsday scenario

Regardless of whether the first round of awards was mishandled, Kim and Sachs say the main problem is that a lot more money is needed.

"I've heard the first round will provide antiretroviral treatment for between 30,000 and 60,000 people," says Kim. "That's a good step, and the first time any money has ever been given for antiretroviral treatment. But now we have to move far beyond that, and come up with much more effective strategies."

The Central Intelligence Agency, Kim notes, recently issued a chilling prediction. A CIA expert has said that the numbers of HIV-infected people in two of Africa's most populous countries are rising so quickly that by 2005, the total number of infected adults on the continent may almost double, rising to 64 million.

That raises the almost inconceivable specter of a continent where fully half the adult population will die an untimely death; where food production has fallen by as much as 40%; and where widespread famine stalks the land. "This is going to be a huge, huge problem," adds Kim.

With only about $700,000 on hand, the fund handed out awards totaling $616 million in April. The grants ranged in size from $93 million for a five-year AIDS program in South Africa to $570,000 awarded to a two-year project in Panama. About 60% of the money went to finance AIDS programs, with the rest divided between TB and malaria programs. The three diseases together account for one in ten deaths that occur each year globally and one in three that occur each year in sub-Saharan Africa.

That's a far cry from what's truly needed, experts agree. According to Sachs, it will take about $8 billion a year to implement what he calls a "comprehensive global program," with elements of prevention, treatment of opportunistic infections, and moderate use of triple-therapy antiretroviral medication.

Though U.S. contributions to the fund total only $300 million so far, there are at least three different bills in the Senate that would increase contributions if they passed:

- Senators Dick Durbin (D-IL) and Arlen Specter (R-PA) are pushing for $700,000 to be tacked onto an emergency spending act that includes billions for military spending.
- In a concurrent move, Senators Jesse Helms (R-NC) and Bill Frist (R-TN) are seeking to add $500 million to the same emergency spending bill. The Helms-Frist money was originally intended for prevention of mother-to-child HIV transmission, but signs from the Helms camp suggest that designating it for treatment of AIDS victims is also acceptable to its sponsors.
- Senators Gordon Smith (R-OR) and Barbara Boxer (D-CA) introduced an international TB control bill that would increase funding for global TB by $200 million. Negotiations are under way to shoehorn the Smith-Boxer bill into the emergency spending bill to create a sort of "superfund bill" for global health.

Emergency spending appropriations become available immediately upon approval, thus bypassing the drawn-out wrangling that accompanies ordinary bills. At least one of the proposals afoot is expected to be approved by November, when the Global Fund will hand out a second round of awards, Hill-watchers say.

In a searing speech delivered to the Senate Foreign Relations Committee last month, Sachs said the U.S. needs to spend much more on infectious diseases globally. Over the past five years, the U.S. has committed only $55 million to fighting AIDS in developing countries, he noted. With less than 0.1% of its gross domestic product committed to all foreign aid, that makes America the stingiest generous donor on earth as measured by percentage of gross national income.

Sachs described a visit he'd made in March to Queen Elizabeth Hospital in Malawi, where 70% of admissions are AIDS-related. "Hundreds of people [were] crowded into the wards to die, two to three to a bed, with patients also lying on the floor under the beds," he said. Yet across the hall in the outpatient ward, the small fraction of patients able to purchase antiretrovirals were being successfully treated, he added.

"The problem in the hospital is not infrastructure, doctors, testing equipment, adherence by patients, or the ability to tell time," Sachs told the senators. "It is simply the shortage of $1 a day per patient that would supply the life-saving drugs." Even when the cost of testing and counseling the HIV-infected is factored in, the sum is less than $3 per day, he added. ■

In a desperate time, Zimbabwe gambles

Despite poverty, antiretroviral therapy planned

Fighting TB in resource-poor African countries hard-hit by HIV must seem like stuffing a thumb into a leaky dike. The sheer numbers of AIDS and TB cases alike grow more astonishing by the day. By 2005, the latest U.S. intelligence analysis suggests, HIV-infected cases in Africa will likely be double what they are today, thanks to logarithmic growth in the epidemic now occurring in two populous countries, Ethiopia and Nigeria.

That raises the specter that by 2005, there will be more than 60 million adults in Africa infected with HIV.

New TB cases soar tenfold

As the epidemic churns across the continent, a conflagration of TB trails in its wake. In Zimbabwe, as one of two or three countries vying for the unenviable title of "nation hardest-hit by HIV," newly diagnosed TB cases have soared tenfold in the past ten years, from 5,000 cases a year to 50,000.

Like most other African countries that are struggling with HIV, Zimbabwe is poor, with a per capita income of under $1,000; accordingly, there are scant resources available for fighting TB and HIV. Botswana and South Africa, also extremely hard-hit, are the two exceptions, with economies placing them on a par with Brazil.

Predictably, Zimbabwe's poverty has crippled the national expansion of directly observed therapy, short-course (DOTS), the treatment strategy for TB approved by the World Health Organization (WHO). According to **Michael St. Louis**, MD, director of the Centers for Disease Control and Prevention's CDC/Zimbabwe AIDS program, nearly one-third of the microscopes in the country have sat broken and useless for years, with no money available for missing parts. In the same way, the cost of transporting supplies and providing supervision has meant that other components of a functioning DOTS program are only partly functional.

To add to the country's TB-related misery, the Netherlands — historically a generous donor with a wealth of TB expertise — has pulled out of both Kenya and Zimbabwe, citing concerns about corruption and human rights violations. The Dutch pullout "is having a major impact on TB programs in Kenya and Zimbabwe," says St. Louis. "Right now, there's no one on the horizon to take their place."

During recent elections, nightly press coverage featured a stream of images of village chiefs proclaiming to campaigning politicians that they required one thing above all others: help in coping with the AIDS epidemic.

The government seems to be listening, St. Louis says. Along with the traditional approaches to taming the co-epidemic — that is, continuing to strengthen DOTS and offering cotrimoxazole (Bactrim) prophylaxis for opportunistic infections other than TB — the health ministry has announced it will pilot antiretroviral therapy, a step once thought to be far too extravagant for so poor a country to attempt.

Serving as technical advisor, St. Louis is helping formulate guidelines for the pilot project. Under his direction, work has also begun to repair the country's tattered microscopy system and shore up its national TB reference lab. The network of volunteers who carry out home-care visits for AIDS victims is also being enlisted to give directly observed therapy to TB patients, St. Louis says.

Finally, cotrimoxazole prophylaxis has been embraced enthusiastically, though it hasn't yet proven its effectiveness here because resistance to the drug hampers its efficacy in some regions, St Louis reports. "People like very much having some positive step they can take," he notes.

Generics help just by existing

Will antiretroviral therapy prove to be feasible in so poor a nation? It helps that the Global Fund to Fight TB, Malaria and AIDS recently gave the country a modest grant for treatment programs, St. Louis says. Although the country won't purchase drugs from a generic maker, the mere existence of generic AIDS drugs has helped bring the price of antiretrovirals down a little, he adds. "Generics have really started the dialogue that has helped bring down prices," he says.

Zimbabwe's decision is only a tentative first step so far. But it may offer a look at the future of the co-epidemics of TB and HIV for the rest of sub-Saharan Africa. No matter what happens, the fact that Zimbabwe is determined to try a first-world solution reflects exactly how desperate the situation has become. ■

Warm weather brings crop of conferences

Hot topics spark TB congress

It's summer. And as surely as songbirds migrate, flowers open, and vegetable gardens are planted, TB conferences bloom across the land.

In Atlanta in May, 24,000 pulmonary and critical-care physicians and researchers converged for the annual American Thoracic Conference. Also, the National TB Controllers Association (NTCA) was scheduled to hold its annual workshop June 18-19 in Fredericksburg, VA. This year's NTCA get-together centered on performance improvement.

One of the starchier-sounding entries on the confab calendar was the 4th World Congress on Tuberculosis, slated for June 3-5 in Washington, DC, which promised to bring almost everyone in TB together to talk about almost everything.

Far from dull, the 4th TB World Congress (the 3rd took place back in 1992) was due to feature some impassioned, even fiery sessions, says **Ann Ginsberg**, MD, PhD, chief of the respiratory diseases branch at the National Institute of Allergies and Infectious Diseases in Bethesda, MD, and a principal organizer of the event. Sessions that seemed sure to throw sparks included talks on multidrug-resistant (MDR) TB, the global epidemic of pediatric TB, and the HIV-TB co-epidemic.

Pediatric TB and the co-epidemic

Jeff Starke, MD, deputy chief of pediatrics at Houston's Ben Taub Hospital, was scheduled to tackle pediatric TB. "That's a problem that's really been ignored," Ginsberg notes. "No one's paid much attention [worldwide] to the epidemiology, since the accepted dogma is that kids don't transmit the disease." Starke, an impassioned orator when it comes to his specialty, was expected to deliver an "eye-opening" report on the subject, Ginsberg says.

As for MDR-TB, it looked as if the "small-envelope" crowd — those who perceive TB resources as limited and who urge pragmatic approaches to global TB control — were due to slug it out again with the "big envelope" opposition, who contend that new paradigms, not more penny-pinching, are what's needed to meet the costly challenge of global MDR-TB.

Then there were sessions on the co-epidemics of HIV and TB, remarkable partly because "there hasn't been very much discussion on the co-epidemic, and I'm afraid the world will pay for our collective lack of attention and effort," Ginsberg says. Talks included how to control TB in a high-prevalence HIV setting, how to use antiretroviral therapy (ART) to staunch the co-epidemic, and the potential for using a DOTS infrastructure to deliver ART.

More broadly, the congress would bring together experts and researchers from disparate areas "who need to hear from each other," Ginsberg says. "It's important to get all these people into the same room — the laboratory researchers, policy-makers, operational people, field workers, and funders — so they can inform each others' thinking," she adds. "That doesn't happen nearly as often as it should in TB. For example, people developing vaccines need to hear from those in the field about what kinds of products can feasibly be delivered." ■

PHRI adds animal lab with New Jersey move

Noted immunologist joins group

The Newark scene may not be as sophisticated as midtown Manhattan. But when the Public Health Research Institute (PHRI, formerly of New York City) cut the ribbon last month for its digs in New Jersey, **Barry Kreiswirth**, PhD, director of PHRI's TB center, says the move felt right.

"Remember, we developed our TB program on the fly in the early '90s," says Kreiswirth, referring to the days when PHRI did the molecular fingerprinting that helped tame the New York TB epidemic. "It's been great to have the luxury to build our new facility exactly the way we want it." That meant going from a three-hooded biosafety level 3 lab to a 12-hooded BL3, he notes. It's also meant snagging Gilla Kaplan, PhD, formerly assistant professor of cellular physiology and immunology at New York's Rockefeller University, and one of the country's foremost TB animal researchers.

"That means we go up a quantum leap," Kreiswirth adds. "Access to animal research

was the one really big arm we were lacking." The TB center's Lattimore Clinic means PHRI will now have access to patient samples as well, he says.

The shop's august new neighbors in the International Center for Public Health include the New Jersey Medical School's National TB Center, the medical school's Department of Microbiology and Molecular Genetics, and its School of Public Health. The massive new building encompasses over 161,000 square feet and was built at a cost of $66 million. ■

Low-incidence guide issued by ACET

Proficiency, resources often pinched

Guidelines tailored to the special needs of low-incidence states — defined as states with a TB caseload of less than or equal to 3.5 per 100,000 — were published last month by the Advisory Council to Eliminate Tuberculosis (ACET). The new guide appeared in the May 3 issue of the *Morbidity & Mortality Weekly Report*.

ACET offered almost a dozen recommendations for the states. Problems in such areas often include lack of expertise, money, and resources, the advisory body says. Yet such areas must continue to shoulder high fixed costs and be ready to cope with not only the occasional case but also outbreaks and even shifting migration patterns that bring populations with a higher incidence of TB or TB latency.

Form partnerships for contact investigations

Among ACET's recommendations are the following:

- Update TB statutes and TB control policy manuals at least every 2 years.
- Maintain an elimination plan designed for local circumstances.
- Form partnerships to ease the burden of labor-intensive contact investigations and targeted testing; likewise, consider adopting case-management techniques for treatment of contacts.
- Consider collaborative arrangements for laboratory services.
- Don't ask local programs for more information than is really needed.
- Consider regionalized approaches to the top-priority function of education and training.
- Let policy-makers know the importance of elimination programs.

More research is needed into several areas of low-incidence policy, ACET adds. For example, more information is needed on regionalized approaches to resource-sharing, whether "face time" can be replaced by distance-based learning and "virtual classrooms," whether costly targeted testing can be cost-effective in low-incidence areas, and what the optimal size is for low-incidence programs.

North Dakota child infected 50 others

Four brief case studies in the document showed several ways outbreaks happen in low-incidence areas. In Maine, a diagnosis delayed for eight months spawned 21 cases; in North Dakota, a child with pulmonary TB infected 50 others (though children are often presumed not to be infectious); in Indiana, drug use and other illicit activities hindered contact investigation; and in Kansas, traditional investigation techniques failed to link cases among exotic dancers and their associates. ■

Gonorrhea rates rising among hardest-hit

HIV infection implications are ominous

At the very time when the nation's syphilis infection rates are declining and new tests make it easier to detect and treat chlamydia, there is a dark cloud on the horizon: More than 60% of the cities that have been hardest hit by gonorrhea infection have experienced increases in the infection rate between 1999 and 2000.

"We see with gonorrhea data continuing challenges with controlling the epidemic," says **Ronald O. Valdiserri**, MD, MPH, deputy director of the National Center for HIV, STD, and TB Prevention of the Centers for Disease Control and Prevention in Atlanta. Valdiserri and other CDC officials presented the latest STD research

and surveillance data at the National STD Prevention Conference, held March 4-7 in San Diego.

"There are 650,000 new cases of gonorrhea every year in the United States," Valdiserri says. "But there also are positive indications that some communities have been able to dramatically reduce new infections."

The increases in gonorrhea infection bodes ill for future HIV infection rates because of the connection between STD infection and increased risk for HIV infection.

"It's a very important point, and it bears repeating, that STD treatment contributes to HIV prevention," Valdiserri says. "A number of studies have documented that having an untreated STD — for someone who's living with HIV — makes the person more infectious to a sexual partner."

Likewise, a person who has an untreated STD and is exposed to HIV has a higher risk of becoming infected with HIV, Valdiserri adds.

"This generally is true not just with gonorrhea, but also with inflammatory STDs, which increase the effectiveness of HIV by two- to fivefold," Valdiserri says.

HIV incidence difficult to measure

Whether increases in gonorrhea rates will lead to increases in HIV rates remains to be seen, and at the present it would be difficult to measure, Valdiserri says.

"We are challenged in our ability to measure the number of new HIV infections in the United States, and we're in the process of developing better ways of measuring HIV incidence," Valdiserri says. "But having said that, we're not seeing increases nationally, although we are extremely concerned about the possibility of increases, particularly in men-who-have-sex-with-men [MSM] populations."

Research and surveillance data presented at the STD conference were mixed. In 2000, syphilis rates fell in 15 of 20 cities that had the highest syphilis rates in 1999, says **Susan DeLisle**, ANRP, MPH, chief of the program development and support branch of the CDC Division of STD Prevention.

There were major declines of greater than 50% in syphilis rates in Tulsa, OK, St. Louis, Richmond, VA, and New Orleans, while there were increases in syphilis rates in Chicago, Detroit, Miami, Newark, NJ, San Antonio, and San Francisco, DeLisle says.

"Increases in some areas remind us that continued vigilance is required in every community if we hope to eliminate this disease," DeLisle says.

Nationally, the syphilis rate declined from 2.4 cases per 100,000 to an all-time low of 2.2 cases per 100,000 in 2000, DeLisle adds.

At least one abstract presented at the conference indicates that the pockets of increased syphilis rates within the context of an overall decline by 90% in the past decade are the result of increases of syphilis infection among MSM.[1]

Rise in syphilis may indicate increase in HIV

"Because syphilis increases the likelihood of acquiring and transmitting HIV infection, and because a large proportion of MSM with syphilis in these outbreaks are HIV-positive, the rise in syphilis among MSM may indicate an increase in the incidence of HIV infection," the abstract states.

Another abstract showed that while primary and secondary syphilis rates declined dramatically in New York City from 58.2 per 100,000 in 1990 to 1.67 per 100,000 in 2000, there has been an increase in the number of syphilis cases among MSM, and many in this population are co-infected with HIV.[2]

Some findings suggest an increase in high-risk behaviors among MSM, such as studies showing a resurgence of gonorrhea and syphilis among MSM in Chicago and Boston and an abstract detailing the practice of "barebacking" (having unprotected anal sex with a non-primary partner) in San Francisco.[3,4,5]

Increases in infection rates of genital herpes (HSV-2) and human papilloma virus (HPV) among MSM populations also are major concerns, says **Stuart Berman**, MD, chief of the epidemiology and surveillance branch of the CDC's Division of STD Prevention.

Correction

The May issue of *TB Monitor* misnamed **Jon Tillinghast**, MD, MPH, state TB controller of Oklahoma. The error occurred in an account of how Oklahoma TB controllers moved quickly to staunch an outbreak, probably preventing many secondary cases by hard work and good contact investigation **("Oklahoma mopping up long trail of TB cases," p. 51)**. *TB Monitor* regrets the error. ■

"More than 6.5 million people become infected with genital herpes and HPV each year," Berman says. "In the United States, 38% of MSM have been infected with HPV type 16, and this is five times the heterosexual male rate and twice the rate of women."

HPV-16 exposure can cause serious problems for a person who has HIV and whose immune system is compromised, Valdiserri says. This is why the CDC is concerned about anal cancer among HIV-infected MSM populations.

"We certainly want to get the message out to sexually active MSM that exposure to this virus has been associated with increased rates of anal cancer," Valdiserri says.

Also, the prevalence of HSV-2 is higher among MSM than among other men, with rates of 31% vs. 18%, although the difference was not statistically significant in a study that surveyed people ages 17 to 59 from 1988 to 1994.[6]

The study concluded that MSM are at higher risk for HPV-16 and probably are at higher risk for HSV-2 infection, although the latter has not been proved.

"Herpes remains a very important problem in the United States," Berman says. "One in five Americans are infected with genital herpes, and men and women who have herpes are five times more likely than uninfected individuals to acquire HIV infection if they're exposed to that virus in sexual contact."

Urine test for chlamydia now available

Because chlamydia traditionally has been associated with severe reproductive health consequences for women and because it's easier to diagnose in women, it hasn't been routinely screened among men, but this could change, DeLisle says. There's a urine test now available, whereas before men would have had to subject themselves to a urethra swab, DeLisle says.

In studies where men are being tested, there are double-digit rates of chlamydia infection among men in the 20-24 age group and among women in the 15-19 age group.

"With the availability of technology that allows for broader screening, we should have additional data," DeLisle says.

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CE/CME

18. Unlike the tuberculin skin-test, there's nothing subjective about the Quantiferon test's reading. What is subjective, however, is:
    A. The cost of the test
    B. The determination of what risk category a subject should be placed in
    C. The impact some medications may have on the test
    D. All of the above

19. Because the new Quantiferon test uses a one-step blood draw, it doesn't require subjects to return two to three days later for a reading, as does the tuberculin skin test.
    A. True
    B. False

20. According to the Central Intelligence Agency, how many people could be infected with HIV in Africa by 2005?
    A. 24 million
    B. 38 million
    C. 64 million
    D. 72 million

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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. ■