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# AIDS ALERT

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Special Coverage of the 2000 Infectious Diseases Society of America Conference

# Clinical care of HIV patients needs comprehensive approach

*Comorbidities, drug reactions complicate treatment*

While there were no earth-shattering breakthroughs or discoveries on HIV presented at the recent Infectious Diseases Society of America (IDSA) conference, the HIV-related presentations made it clear that clinicians have reached a fork in the road of HIV care. They may continue with the piecemeal approach to care that focuses primarily on the HIV disease itself, or they can enter the new age of HIV treatment that calls for caregivers to treat all of the HIV patient's medical needs.

Much of the new research presented at the Sept. 7-10 conference in New Orleans involved studies of HIV patients with comorbidities and medical problems that may or may not be the result of sustained antiretroviral treatment. **(See story outlining some of the IDSA research, p. 144.)**

"We have for a long time in HIV care focused our attention on opportunistic infections and antiretrovirals," says **M. Keith Rawlings**, MD, associate medical director of Parkland Health and Hospital Systems at Southeast Dallas Health Center.

"Now these same clinicians have to be more and more attuned to general medical management of the patient's hypertension, diabetes, and other kinds of medical management issues," Rawlings notes.

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## COMING IN FUTURE ISSUES

■ **Are patients ready for HIV meds?** Study assesses patient motivation for adhering to antiretroviral drug regimens

■ **Learning how to treat cachexia:** Studies shed light on what causes cachexia and how best to treat it

■ **Name-based HIV reporting:** Researchers find that such policies do not deter testing, but may be associated with delaying it

■ **HIV drug interactions pose big challenge:** New studies highlight confusing drug interaction problems, emphasizing the importance of additional clinical research

■ **Watch for risk factors of CMV retinitis:** AIDS patients undergoing antiretroviral therapy are at risk of unilateral advancement of cytomegalovirus retinitis

For instance, the increase in the number of women with HIV means HIV clinicians will now be caring for more women patients, who will need regular Pap smears, Rawlings suggests.

Another study introduced at the IDSA conference that examined the incidence of cervical carcinoma in HIV patients found a trend of a higher incidence of the disease in HIV-infected women from 1996 to 1999 than from 1992 to 1995.[1] While not statistically significant, the increase at least suggests it's a good policy to recommend annual Pap smears to HIV-infected women.

"Perhaps clinicians should adhere to a recommendation of yearly Pap smears for HIV-infected women and have a more vigilant attitude toward minority groups such as Hispanics and African-Americans," says **Regis Vilchez**, MD, a research fellow and member of the Baylor Center of AIDS Research at the Baylor College of Medicine in Houston. Vilchez was an investigator on the study of four AIDS-related malignancies.

### *Kaposi's sarcoma incidence has declined*

The malignancy study confirmed that the incidence of Kaposi's sarcoma decreased significantly in the later period when highly active antiretroviral treatment (HAART) became available. But there was a statistically insignificant decrease in non-Hodgkin's lymphoma and a statistically significant increase in the incidence of Hodgkin's disease.

"It is a complicated issue, but in light of observations, it appears antiretroviral therapy influences Kaposi's sarcoma. But we cannot conclusively say it has had an impact with the other malignancies," Vilchez says.

The Centers for Disease Control and Prevention in Atlanta also published research this year in the *Journal of Acquired Immune Deficiency Syndrome*, confirming that the incidence of Kaposi's sarcoma has been declining in the United States due to combination antiretroviral therapies.

However, HAART hasn't eliminated Kaposi's sarcoma and apparently has no impact on the three other malignancies included in the Baylor study. The fact that HIV patients continue to develop serious malignancies is an important point to consider when treating this population, Vilchez says.

"AIDS-related malignancies are an important component of the opportunistic infections [OIs] that one can expect in patients on HAART," he

says. "Indeed, malignancies have become the most important cause of mortality among AIDS patients in the United States."

Malignancies are now more important causes of death among the AIDS population than are pneumonia, cryptococcal meningitis, and progressive multifocal leukoencephalopathy, Vilchez adds.

However, HAART still is relatively new, and decades from now it's possible HIV patients will die of comorbid conditions, such as heart disease and diabetes, more readily than they do of OIs, some experts say.

"If you think about it, HIV behaves more like a chronic medical disease than it does an infectious disease, and in many cases what we're now asking our HIV experts to be is primary care physicians, and not just for HIV, but for all medical problems," Rawlings adds.

Rawlings was a chief investigator of a study that analyzed the comorbidities and clinical indicators of a group of HIV-positive patients between 1996 and 1999. Investigators found that there was an increase in the average number of comorbid conditions among the 335 patients in the cohort study. The average number of comorbidities per patient increased from 1.11 in 1996 to 1.92 in 1999. The percentage of patients who had no comorbidities decreased from 33.7% in 1996 to 15.2% in 1999.[2]

"The notion that we have this population that has nothing wrong with them except HIV isn't really true," Rawlings says. "The number of things that were wrong with them as a comorbid issue, not as a side-effect issue, was increasing."

## HAART may not be to blame for comorbidities

The Dallas study draws no conclusions about the cause of the increase in comorbidities. Rawlings says he doesn't believe it's valid to assume comorbidities have increased as a side effect of HAART.

"If you're seeing more and more women becoming infected, it shouldn't be surprising that you're having more hospitalizations for pregnancy and cervical dysplasia," Rawlings says. "And if you're seeing more and more minorities, then it shouldn't be a surprise that there are more hypertension and hyperlipidemia cases."

Regardless of whether the comorbidity increase is a result of changes in patient demographics or the use of HAART, the fact remains that the nature of HIV care is changing, Rawlings adds.

For example, HIV clinicians now also need to be aware of the possibility of osteoporosis or other bone diseases among their patients. This is a disease that may never been considered an issue even worth mentioning pre-HAART.

National Institutes of Health (NIH) research and other recent studies have suggested that HIV patients on HAART may be at greater risk for developing osteonecrosis. **(See "Studies link bone disease, antiretroviral meds," *AIDS Alert*, November 2000, p. 137.)**

Additionally, a pilot study conducted at the University of North Texas Health Science Center in Fort Worth showed decreased bone density and an increased risk of fracture among a small cohort of HIV-infected patients.

## HIV patients had other comorbidity risk factors

"Many women in the study were predisposed to having osteoporosis separate from whether they were HIV-infected," says **Bernard R. Rubin**, DO, professor of medicine and chief of the division of rheumatology at the University of North Texas Health Sciences Center.

Some of the women were post-menopausal, and others had anorexia, bulimia, a poor dietary intake of calcium, or a strong family history of bone loss, Rubin says.

HIV-infected men included in the pilot study also had signs of decreased bone density. Most of the time, the cause is hypogonadism, Rubin adds.

The research suggests that people severely ill with HIV are prone to bone disease independent of their age. The average age of the 12 women and 17 men included in the study was 33 years. Bone scans were abnormal in 16 people who were less than 40 years of age.[3]

"We found people in their 20s and 30s with bones as brittle as older people," Rubin says.

Researchers are continuing the study, looking at a larger population of 60 patients, says **Barbara A. Atkinson**, DO, a co-author of the abstract and chief of infectious disease and associate professor at the University of North Texas Health Sciences Center.

Atkinson cautions clinicians not to draw too many conclusions about changing treatment based on the limited study, but to continue to follow osteoporosis guidelines of scanning all post-menopausal women for bone density loss.

There are treatments available for male and female HIV patients who have osteoporosis or bone density loss. These include Alendronate, which has been approved by the U.S. Food and Drug Administration for management of post-menopausal osteoporosis.

"Alendronate is not a hormone, and it works in men, too," Rubin says. "So now we have a drug for either sex."

Other HIV research relating to comorbidities and OIs presented at the IDSA conference included a study of cardiovascular risk in HIV-infected people and a look at progressive multifocal leukoencephalopathy (PML) in the pre-HAART and post-HAART eras. **(See story on PML, p. 146.)**

The cardiovascular study, coming from the University of Cincinnati College of Medicine, concluded that HIV-infected patients may have cardiovascular disease, but it's associated with traditional risk factors. That study found no clear evidence that using protease inhibitors increased patients' risk for cardiovascular disease.[4]

### *Team approach may work best*

With the strong possibility that HIV patients may have comorbidities, such as heart disease, bone density loss, PML, or malignancies, clinicians probably are best off treating these patients through a team approach, Vilchez and Rawlings say.

"There will have to be a dual-management approach, so it's important for me to have access to a cardiologist who is familiar with HIV management, and I need to be familiar with the cardiovascular management, so we are able to provide care that is appropriate for the entire spectrum of illness that a patient has," Rawlings says.

Rawlings, who has worked with HIV patients for more than a decade, often has HIV-infected patients referred to him who have diabetes, high blood pressure, and heart disease. "If a colleague identifies an HIV-positive patient, they will refer that patient to me and my team to follow this individual, even if HIV is the least of this patient's problems," he notes.

While Rawlings chooses to provide general medical care to HIV patients, some physicians live in areas where there are few alternatives. These physicians have little choice but to provide most of the medical care their HIV patients need, and they especially need to be aware of comorbidities and the changes among OIs, Vilchez says.

"This was a point brought up at IDSA: A substantial number of physicians taking care of HIV infection are generalists, individuals who have been trained as family or internist physicians," Vilchez says. "They have the load of taking care of these patients in rural or suburban areas, and I believe they need to be aware of this issue."

### *References*


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2. Rawlings MK, De Guzman C, Slaker R, et al. Comorbidity and clinical indicators in a cohort of 335 HIV+ patients 1996-1999. Abstract #324 presented at the Infectious Diseases Society of America conference. New Orleans; Sept. 7-10, 2000.
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***Special Coverage of the 2000 IDSA Conference***

# IDSA research shows change in HIV progression

*Opportunistic infections highlighted*

The recent Infectious Diseases Society of America (IDSA) conference, held Sept. 7-10, 2000, in New Orleans, presented a body of research on HIV that demonstrates how investigators anticipate major changes in the course of HIV treatment.

Much of the research focused on HIV patients' comorbidities and opportunistic infections in the age of highly active antiretroviral therapy (HAART).

Here is a brief summary of some of the abstracts presented at the conference:

• **Pneumococcal infections:** Investigators from the Centers for Disease Control and Prevention in Atlanta, Johns Hopkins University in Baltimore, and the University of Pittsburgh presented an abstract on a study of recurrent invasive pneumococcal infections in HIV-infected patients.

Their research found that most patients who have recurrent pneumococcal disease have been reinfected with a new strain. All of the strains found to be involved in relapsing disease are included in the 23-valent pneumococcal polysaccharide and the 7-valent pneumococcal conjugate vaccine.[1]

• **Latent tuberculosis infection:** Researchers from Emory University and Emory University School of Medicine in Atlanta investigated the optimal time to perform purified protein derivative (PPD) testing to identify latent tuberculosis infection after the initiation of HAART.

Investigators found that a patient's current CD4 cell count is the best predictor of the patient's ability to respond to delayed-type hypersensitivity skin testing, and PPD testing should be considered once a patient's CD4 cell count exceeds 100 cells / $mm^3$ after treatment with HAART.[2]

• **Comorbidity among HIV patients:** Investigators at Parkland Health and Hospital System in Dallas and Clinical Partners of San Francisco analyzed trends in HIV clinical status and number and type of comorbidities in a cohort of 335 HIV-positive patients between 1996 and 1999.

Investigators assessed these 17 key comorbidities: treatment with antidepressants / antipsychotics, cardiac arrhythmia, cervical dysplasia, diabetes, heart failure, hepatitis, herpes, hyperlipidemia, hypertension, ischemic heart disease, kidney stones, lipodystrophy, necrosis, non-PCP pneumonia, pregnancy, chronic respiratory disease, and tuberculosis.

The study concluded that as HAART use increased, patients' HIV clinical status improved, but the average number of comorbidities per patient increased dramatically.[3]

• **Increasing incidence of steatohepatitis and lactic acidosis:** A researcher at St. Vincent's Hospital and Medical Center in New York City investigated obesity-related, nucleoside analog-associated steatohepatitis and lactic acidosis in HIV-infected patients.

The study, which focused on six cases of steatohepatitis and lactic acidosis among obese, HIV-infected patients, suggests that obesity might be a predisposing factor for mitochondrial dysfunction in HIV-infected patients treated with nucleoside analog reverse transcriptase inhibitors (NRTIs). Therefore, clinicians might wish to consider NRTI therapy to be contraindicated in some obese HIV-infected patients.[4]

• **Cardiovascular risk in HIV patients:** Researchers from the University of Cincinnati College of Medicine investigated whether HIV-infected people were at risk for the development of ischemic cardiovascular disease (CVD) due to treatment-associated metabolic complications, underlying cardiovascular risk factors, or other mechanisms.

They conducted a retrospective, case-control study of 15 HIV-infected patients with proven CVD who were seen between April 1, 1999, and April 25, 2000. The control group included HIV-infected patients who had no known CVD but who were similar in age and gender the control group. The investigators found that when compared to the control group, the HIV patients with CVD had more pre-existing risk factors and a lower nadir CD4+ lymphocyte count. This study found no clear association between the use of protease inhibitors and the occurrence of CVD.[5]

• **Loss of bone mass:** Investigators at the University of North Texas Health Sciences Center in Fort Worth assessed 29 HIV-infected people for their degree of bone loss in a pilot study.

Using dual energy X-ray absorptiometry, investigators found abnormal scans in 16 individuals who were less than 40 years of age. Men at greatest risk of fracture in the femur had CD4 cell counts of less than 200 cells / $mm^3$. While not identifying any causes of the decreased bone density, the study suggested that additional investigation should clarify the incidence of bone loss among HIV patients and also determine whether progressive loss occurs over time.[6]

## *Incidence of Kaposi's sarcoma has declined*

• **Four AIDS-related malignancies:** Baylor College of Medicine in Houston researchers studied the impact of antiretroviral therapy on the incidence of four AIDS-related malignancies, including Kaposi's sarcoma, systemic non-Hodgkin's lymphoma, Hodgkin's disease, and cervical carcinoma.

Investigators found that the incidence of Kaposi's sarcoma has significantly declined since the advent of HAART, but there was no similar finding in the incidences of the three other malignancies.[7]

In the period 1992-1995, the incidence of Kaposi's sarcoma was 12.4 per 1,000 person-years, compared with 9.4 per 1,000 person-years in the 1996-1999 time period. For non-Hodgkin's lymphoma, the 1992-1995 incidence was 8.6 per 1,000 person-years, and the incidence in 1996-1999 was 6.5 per 1,000 person-years. In 1992-1995, the incidence of Hodgkin's disease was 0.7 per 1,000 person-years, compared with 1.3 per 1,000 person-years in 1996-1999. And for cervical carcinoma, the 1992-1995 incidence was 0.2 per 1,000 person-years , compared with 0.9 per 1,000 person-years in the 1996-1999 time frame.

• **Lactic acidosis in hospitalized HIV patients:** A second study examining lactic acidosis, this one from the University of Alabama at Birmingham School of Medicine, assessed the clinical features and incidence of lactic acidosis among hospitalized HIV-infected patients who had been on NRTI therapy.

Investigators reviewed cases from January 1995 to February 2000 and found 12 subjects who presented with either abdominal pain or nausea or emesis. The study concludes that there are an increasing number of lactic acidosis syndrome cases in NRTI-treated HIV-infected subjects, which could reflect cumulative long-term toxicity.[8]

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*Special Coverage of the 2000 IDSA Conference*

# Once uniformly fatal, PML now less dangerous

*Research says treat early for best results*

Progressive multifocal leukoencephalopathy (PML) was a relentless harbinger of imminent death among some AIDS patients in the first 15 years of the HIV epidemic. Following PML diagnosis, AIDS patients could expect to die within a year.

But the situation has changed since 1996 and the advent of highly active antiretroviral therapies (HAART), according to research presented at the Infectious Diseases Society of America conference held in September in New Orleans.

Researchers at the University of Rochester (NY) conducted a retrospective chart review of patients with AIDS-associated PML who were hospitalized from January 1980 to March 2000. They found 34 patients with PML, including three for whom PML was the first HIV manifestation. PML is a demyelinating disease of the brain caused by the JC virus, which is a polyomavirus of the papovirus family. Its symptoms include palsies, seizures, dysarthria, cranial nerve deficits, cortical blindness, quadriparesis, profound dementia, aphasia, and ataxia. **(See related story in "AIDS Guide for Health Care Workers," inserted in this issue.)**

Those diagnosed in the pre-HAART era had a mean survival time of 309 days after onset of symptoms, vs. those on HAART, who had a mean survival time of 557 days.[1]

"We wanted to see if antiretrovirals caused any change in PML deaths," says **Bogdan Neughebauer**, MD, PhD, instructor and fellow in medicine, infectious diseases, at the University of Rochester Medical Center. Neughebauer was an investigator on the study.

"The most interesting thing was that there was a very clear advantage for patients on HAART," Neughebauer says. "Those compliant with HAART lived much longer than the patients not on HAART."

Of the PML patients receiving HAART, six are still living some five or six years after their diagnosis. This is remarkable when considering the fact that AIDS patients with PML who receive no antiretrovirals typically die within three to six months, Neughebauer says.

"So you can understand our excitement," he adds. "There are patients who survived spontaneously, and this shows that HAART is really doing the job — it's not a coincidence."

When HIV patients were divided according to whether they were on monotherapy, two antiretrovirals, or three or more combination therapies, researchers found that patients on combination therapies lived longer than those on one or two antiretrovirals, Neughebauer says. "And that group lived longer than those who didn't take any medications," he adds.

The study's findings were that patients on no antiretrovirals or who had documented nonadherence lived an average of 126 days, those on mono- or dual therapy lived an average of 445 days, and those on HAART lived an average of 792 days.

There was one subgroup of PML / HIV patients included in the study who lived only 60 days despite receiving HAART. This group had been started on HAART too late, when the PML was at its peak according to symptoms, Neughebauer says.

"Our suggestion is that if you have a patient who has a bit of confusion, an MRI should be done," he says. Also, clinicians should perform a polymerase chain reaction test to identify the JC virus.

HAART has no direct effect on the JC virus, but by suppressing HIV, it permits the patient's immune system to fight the JC virus effectively, Neughebauer says.

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# Pharmacy records reveal patient med adherence

*Study concludes that patients inflate self-reports*

Patients will say they're taking their medications regularly, but if their viral loads are rising and CD4 cell counts are falling, it's a good idea to double-check their self-reports.

A study of 100 HIV patients receiving care through the Denver Public Health system demonstrated that nonadherence is relatively common.[1]

"Not all that surprisingly, there wasn't a great correlation between self-reported adherence and pharmacy adherence," says **William J. Burman**, MD, attending physician in the Infectious Disease Clinic of Denver Public Health.

"If you take pharmacy adherence to be a more accurate measure, then patients more often overestimated their adherence than they underestimated it," Burman says. "And clinicians can't predict which patients will have adherence."

Investigators at Denver Public Health did an earlier study of patient adherence to a pneumocystis prophylaxis. That study found that nonadherence was common and not well-predicted by clinicians, Burman says.

"Clinicians need, if at all possible, objective data to diagnose problems with adherence," he says.

The most objective data come from the pharmacy. But if a clinician doesn't know where patients are filling prescriptions, then it's possible to obtain a more accurate self-report by asking patients more specific questions.

"Don't ask, 'Do you take your medications correctly?'" Burman says. "What's more helpful is a very focused questionnaire about the past three days, because generally the accuracy of self-reported data is greater if you ask very specific questions."

At Denver Public Health — a large urban public health system — pharmacy adherence is fairly easy to monitor. The health system serves mainly low-income and indigent patients who fill their prescriptions at one pharmacy. It's easy to identify which patients have been filling their prescriptions and which haven't.

"When we're faced with a patient with rising viral loads, the first question we ask is, 'What have they been doing with their old drugs,' and quite often that answer is very revealing," Burman says.

"Our attitude is that if there were problems with adherence with the old regimen, unless you do something about that, there will be more problems with adherence in the salvage regimen," he adds.

The study found that of 81 patients on therapy, 56, or 73%, were adherent by a 3-day recall, and 48 or 59% were adherent according to pharmacy data. Self-reported nonadherence risk factors

were alcohol abuse, life stress, and Hispanic ethnicity. Pharmacy nonadherence risk factors were African-American or Hispanic race/ethnicity and a history of injection drug use. Patients in the study reported that the most common reasons for missing doses were being busy (48%), forgetfulness (42%), "don't feel like taking medication" (32%), and side effects (22%).[1]

Denver Public Health investigators surveyed patients on what obstacles and solutions were related to their adherence. "We took a lot of the patients' suggestions," Burman says.

For example, Denver Public Health clinicians dispense medications whenever possible and give pillboxes to all patients who want them. Also, Denver Public Health has an outreach team that pays weekly visits to patients who ask for help with adherence, he says.

"One of the lessons from the research was that life stress was really correlated with adherence," Burman says. "The message to clinicians is that we must deal with major problems before starting patients on antiretrovirals, and these problems include depression, substance abuse, social issues, and housing issues."

Burman also suggests that physicians be prepared to refer some patients to psychiatric care. "We consider that to be part and parcel of primary medical care."

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# CDC issues ambitious goals for reducing HIV infections

*Draft plan draws both praise and criticism*

The Centers for Disease Control and Prevention in Atlanta placed its formidable goals for preventing new HIV infection in the national political arena this fall, and already the draft document has created a stir among Congress, supporters, and critics.

The CDC's goal to reduce new HIV infections in the United States from an estimated 40,000 per year to 20,000 could cost as much as $1 billion annually, according to scientific reports quoted in the CDC's draft plan. The CDC's prevention budget for fiscal year 1999 was $637 million.

Research presented at the International AIDS Conference held in Durban, South Africa, in July 2000 estimated that just to provide prevention services to at-risk injection drug users in the United States would cost $423 million a year.

"We at the CDC recognize that these are ambitious goals, and they won't be easily obtained, but we do think it's possible with appropriate focus and resources to reduce new infections in this country by half," says **Ron Valdiserri**, MD, MPH, deputy director of the National Center for HIV/STD/TB Prevention at the CDC. **(See chart detailing CDC goals, p. 149.)**

Even this ambition does not go far enough, some critics charge.

"It talks about reducing new infections, but not eliminating them," says **George Bellinger Jr.**, program director for the Harlem Directors Group in New York City.

"My overall opinion is that the CDC's plan looks like a very good HIV care document because it focuses more on people already living with HIV rather than preventing HIV," Bellinger says.

For instance, the CDC's third goal is to increase the proportion of HIV-infected people in the U.S. who are linked to appropriate care. **(See Goal No. 3 objectives and strategies, p. 150.)**

"That's fine," Bellinger says of this goal. "However, if the CDC spends its money on locating and educating HIV-positive individuals about AIDS, that's what the Ryan White funding is for."

Bellinger suggests a better prevention goal would be to increase the number of HIV-positive people involved in the implementation of prevention strategies. "This is so people who are positive will be involved with prevention strategies to educate other people about the risk of transmitting HIV," he says.

Others say the plan is laudable simply because it gives politicians and others a concrete plan for reining in the epidemic.

"It's going to be a very useful tool with Congress in the sense that it finally puts a tangible goal out there," says **Julio Abreu**, deputy director of government affairs for AIDS Action, an AIDS advocacy group in Washington, DC.

In fact, Congress already has taken note of the plan, says **Steve Morin**, PhD, an associate

professor of medicine at the University of California-San Francisco. Morin was one of the more than 100 experts who helped write the five-year strategic plan.

"This is exactly the kind of tool that is needed to build confidence that if you invest more money in prevention, it will be spent wisely with measurable outcomes and performance indicators," Morin says.

Capitol Hill briefings have already made mention of the CDC's plan, he says. "And the labor, health, and education bill may include a significant increase to respond to this plan, so it's made a difference already."

CDC officials are revising the plan, taking into consideration comments made by HIV service organizations, clinicians, and others, and the final plan is expected to be released in January.

AIDS service organizations and others will look at the comments the CDC receives on the plan and how these are incorporated into the final document.

"We want to see if these comments make sense and if we can strengthen the document," says **A. Cornelius Baker**, executive director of the Whitman-Walker Clinic in Washington, DC. "I think the document is clearly written and the plan is heading in a good direction, but I think we all want to make sure it's not just a good, well-written document that's not used."

### *Plan addresses needle-exchange programs*

For instance, the CDC's draft plan includes a priority objective of increasing the proportion of injection drug users (IDUs) who abstain from drug use or who use harm-reduction strategies to reduce their risk of HIV transmission or acquisition. One of the selected strategies listed under that objective reads, "Continue to disseminate scientific evidence that needle-exchange programs are effective at reducing HIV infection while not increasing drug use."

That's fine, but it doesn't solve the problem that the federal government has been actively opposed to needle-exchange programs, Baker says.

"This plan is going to require bold leadership, because there are areas where we need to be clear that this plan will not succeed if we don't have more enlightened policies on AIDS," Baker adds. "To the extent that the government is not willing to support needle-exchange plans across the country, our ability to impact the HIV infection rate among injection drug users is fairly limited."

At least the plan makes it clear that targeting IDUs is a priority. Some at-risk populations, however, are not even mentioned in the draft plan. For instance, Bellinger questions why the CDC plan fails to identify strategies that target the high-risk transgendered population.

"The plan does not mention transgender individuals at all, and that's important when dealing with men who don't identify as gay or bisexual who may be having sex with men and post-op transsexuals," Bellinger says. "The CDC should mention this issue, bring it out of the closet, and identify resources to address transgender communities."

Despite flaws, some of which may be ironed out in the final plan, the document is likely to serve as a catalyst for increasing funding for HIV prevention, and that's a very positive first step, Abreu and Morin say.

"We've always had difficulty getting adequate funding for CDC prevention efforts," says Morin, who worked for the U.S. House of Representatives' appropriations committee for six years and is very familiar with the CDC's budget.

"A lot of external groups have been critical of the CDC's priorities and programs," he adds.

To answer the criticism, an external budget review group that included Morin met several times last year to analyze how the CDC was spending HIV prevention and surveillance funds.

### CDC's Goals for HIV Prevention

**1.** Reduce the number of new HIV infections per year in the United States from an estimated 40,000 to 20,000 per year by 2005.

**2.** Through voluntary counseling and testing, increase the proportion of HIV-infected people in the United States who know they are infected from the current 70% to 95% by 2005.

**3.** Increase the proportion of HIV-infected people in the United States who are linked to appropriate care, prevention services, and treatment services from the current estimated 50% to 80% by 2005.

**4.** Reduce HIV transmission and improve HIV/AIDS care and support through partnership with resource-constrained countries.

*Source:* CDC's prevention plan, September 2000 draft.

## Goal No. 3 of the CDC's Draft HIV Prevention Plan

| Priority Objectives | Selected Strategies |
|---|---|
| Work with public health, the private medical sector, the Health Resources and Services Administration (HRSA), and other partners to reduce the disparities in access to prevention and care services that are experienced by communities of color and by women. | **1.** Collaborate with HRSA, the National Institutes of Health, the affected communities, and other partners to develop and implement a comprehensive research agenda that identifies and addresses barriers to prevention services and access to care.<br>**2.** Promote cultural and linguistic competence in CDC-funded programs. |
| Work with public health, the private medical sector, and other partners (e.g., the Substance Abuse and Mental Health Services Administration, HRSA) to increase the percentage of people diagnosed with HIV who are successfully linked to culturally competent, science-based behavioral prevention services. | **1.** Assure that HIV-infected people tested in CDC-funded sites obtain a comprehensive prevention assessment and appropriate referral to prevention case management (PCM) within 3 months of learning their HIV status.<br>**2.** Collaborate with HRSA to encourage the establishment and maintenance of behavioral prevention services in public HIV/AIDS outpatient clinics.<br>**3.** Increase the capacity of health care providers to provide behavioral prevention counseling.<br>**4.** Develop a system to monitor HIV-infected patients' linkage to prevention services. |
| Work with public health, the private medical sector, HRSA, and other partners to increase the percentage of people diagnosed with HIV who are successfully linked to care within 3 months of learning their HIV status or of being re-identified as being HIV-infected but out of care. | **1.** Publish guidelines for best practices for linkage from post-test counseling to medical evaluation.<br>**2.** Conduct research to determine why previously diagnosed but currently out-of-care people didn't initially access or remain in medical care and develop interventions to enhance care utilization. |

*Source:* CDC's prevention plan, September 2000 draft.

"The group concluded that it was difficult to know whether the CDC's spending was the best allocation of resources unless you could match it against a strategic plan," Morin says.

There has never been a strategic plan directly linked to a budget, he adds. "So that's what the external budget review group recommended, is that the CDC develop this national plan and try to see how the budget reflected the priorities in the plan."

The CDC enlisted help from more than 100 people, including government employees, community providers, academicians, activists, researchers, and others, to help draft the plan. The large group was divided into four working groups, each of which worked on one of the four goals. The groups identified objectives and strategies that would be necessary to achieve the goals within a five-year time frame, Valdiserri says.

"We will take a close look at our budget to make sure we direct those priorities," Valdiserri says. "We hope to be able to more completely describe to policy-makers what some of the unmet needs are."

Valdiserri says the plan's top priorities are listed first. Under the first goal to reduce the new HIV infection rate, the objectives put programs targeting men who have sex with men and programs directed toward adolescents near the top of the list. This is because the CDC's most recent data show that men who have sex with men still account for the greatest proportion of new HIV infections.

Likewise, the CDC estimates that more than half of all new HIV infections are among people under age 25, and the majority of these people have become infected through sexual activity.

The CDC, with help from providers, Congress, and U.S. citizens, should be able to make the prevention plan a reality, Valdiserri says.

"We have the science to achieve these goals," he adds. "If we have the national will and adequate resources, we can achieve them, and that's an issue that all of America needs to address because it's not just a CDC issue." ■

# Physician empathy affects HIV patient satisfaction

*Research looks at what patients really want*

HIV-infected patients will be more satisfied with their physicians if they perceive that their doctors are showing empathy and are knowledgeable about HIV, according to a recent study.[1]

"It's the quality of patient-doctor communication that drives patient satisfaction," says **Jeffrey Samet**, MD, MPH, associate professor of medicine and public health at Boston University Schools of Medicine and Public Health. Samet was the study's principal investigator.

Patient satisfaction has become a more important issue in medicine in recent years, and HIV patients are no exception. Patients who are pleased with their medical care are more likely to be adherent to their treatment regimens and often have improved clinical outcomes, according to earlier research.

"There are a lot of reasons why one would like to enhance satisfaction," Samet says. Physicians would want to enhance customer satisfaction to demonstrate better clinical outcomes and to improve their quality report cards with managed care companies.

The study involved 203 HIV-infected patients who were assessed at baseline and divided into four categories: sociodemographic, HIV risk, alcohol and drug use, and health status and quality of life.

At six months, 146 of the original 203 patients were interviewed. Investigators measured their satisfaction by asking them two questions: "Does your primary care physician meet your expectations?" and "How satisfied are you with your primary care physician?"1

Patients were asked to respond on a four-point scale that included these responses: completely, somewhat, a little, and not at all. Patients' responses were summed and scaled from 0 to 100.

The study found that 56% of patients were nearly completely satisfied with their physician, meaning that their answers to the two satisfaction questions were either "completely" and "completely," or "completely" and "somewhat."

There was an association between patients' satisfaction levels and some of their answers to a long list of other questions related to their medical care. But there was no association between satisfaction and any of the sociodemographic characteristics of patients or to their risk factors, health status, or alcohol and drug use, Samet says.

"The important qualities of primary care physicians had to do with how they communicated with their patients," he says.

This finding was different from previous studies, which did find a significant association between a patient's characteristics, the characteristics of the site of care, and overall satisfaction.

Here are some of the other issues that investigators asked patients to address at the six-month follow-up interview:

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**Editorial Questions**

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• Rate the convenience of their clinic's hours.

• Was there one doctor's office/clinic where the patient received most of his or her care?

• Did the patient see one doctor, nurse, or physician's assistant at this office/clinic?

• How comfortable was the patient in discussing personal issues with the primary care physician?

• Were there relationship problems with the primary doctor?

• How well do patients understand what doctors tell them about the HIV illness and medications?

• How sympathetic is the primary care physician to what patients are going through?

• How well does the physician listen to patients?

• How often does the doctor ask for patients' input when making medical care decisions?

• How often does the doctor ask about patients' personal relationships?

These issues were strongly associated with patient satisfaction with the physician's care:

• The patient found the clinic hours to be more convenient.

• The patient was comfortable discussing personal issues with the doctor.

• The patient understood the physician's instructions.

• The physician demonstrated empathy.

• The patient participated in the medical encounter.

• The physician showed an interest in the patient's personal relationships.

• The patient perceived the physician to be very knowledgeable about HIV.

If clinicians can draw any conclusions from this study, it might be that they should work on improving their patient-doctor communication, Samet says.

"It's not a gift that we were born with, although some may be naturally more talented in that realm," he says. "But it can be improved by training."

Physicians who choose to enhance their own skills in the realm of patient-doctor communication may improve their encounters with HIV patients and these patients' satisfaction with those interactions, Samet adds.

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## CE objectives

After reading this issue of *AIDS Alert*, CE participants should be able to:

• identify the particular clinical, legal, or scientific issues related to AIDS patient care;

• describe how those issues affect nurses, physicians, hospitals, clinics, or the health care industry in general;

• cite practical solutions to the problems associated with those issues, based on overall expert guidelines from the Centers for Disease Control and Prevention or other authorities and/or based on independent recommendations from specific clinicians at individual institutions. ■

AIDS GUIDE
For Health Care Workers®

# HIV patients who have PML can now live for years

*Patients will live longer with PML if they are diagnosed and treated early*

Before the introduction of antiretroviral treatment and combination therapies containing protease inhibitors and other powerful HIV medications, AIDS patients who developed progressive multifocal leukoencephalopathy (PML) typically would die within three to six months.

This severe neurologic disease progressed rapidly in AIDS patients, causing muscle weakness; spasms; blurred or double vision; difficulty with walking, swallowing, and speaking; headaches; confusion; poor concentration; and sometimes blindness.

Recent studies suggest that some HIV patients who are diagnosed with PML early in the disease have survived for more than three years while receiving combination antiretroviral therapy.

However, at least one study has found that the survival rate is greatest when the patients are not in advanced stages of HIV disease and PML disease. This is why it's very important for clinicians to diagnose PML as early as possible.

Here is some information about PML, its diagnosis, and its treatment:

• **What is progressive multifocal leukoencephalopathy?**

This rare AIDS-related condition is caused by the JC virus, which is a polyomavirus of the papovavirus family. The JC virus is believed to have infected up to 90% of adults, so infection cannot be prevented. However, it only develops into a fatal demyelinating disease of the brain in people who are severely immunocompromised.

A chronic progressive illness, PML causes patients to decline rapidly, usually resulting in dementia, encephalopathy, coma, and death.

Most cases of PML occur in people with AIDS whose CD4+ cell counts are very low, such as people with CD4 counts of less than 90 cells / $mm^3$.

In PML, the JC virus infects the brain, forming lesions. There is no standard course of the disease because there's no way to predict which part of the brain the virus will strike first. For instance, if the virus first infects the part of the brain that controls speech, the first sign of PML disease in that patient would be aphasia. But in another person, the virus could first infect the part of the brain that affects eyesight, so that person's first symptom would be a change in vision.

• **What are PML's symptoms and how is it diagnosed?**

Symptoms include muscle incoordination, cranial nerve deficits, cortical blindness, gait abnormalities, personality changes, fever, confusion, paralysis on one side, and speech difficulties.

PML cannot be diagnosed solely by symptoms or by a magnetic resonance imaging (MRI) brain scan, because other AIDS-related opportunistic

infections present similar symptoms and MRI results, such as toxoplasmosis, AIDS dementia complex, lymphoma, cytomegalovirus, herpes infections, and cryptococcal meningitis. Because a majority of adults have antibodies to the JC virus, it's also not useful to conduct blood or urine tests as a diagnostic tool.

Clinicians may suspect PML when a computed tomography (CT) or MRI scan shows multiple areas of cerebral white matter demyelination. But a more specific diagnosis requires a biopsy of brain tissue.

There is new research suggesting that a polymerase chain reaction (PCR) analysis of cerebrospinal fluid will enable a diagnosis of the disease in a majority of cases. But clinicians now are using PCR testing in conjunction with a brain biopsy.

Patients may be reluctant to have a brain biopsy because of the procedure's invasiveness. However, if PML is suspected, the biopsy is recommended, because it can rule out other common brain diseases that may be treatable.

**• How is PML treated?**

Until recently, there were no effective treatments, and patients who had this illness could expect to die very soon after diagnosis. This dismal prognosis has changed since the introduction of protease inhibitors and combination antiretroviral therapies for HIV patients.

The key to preventing the JC virus from infecting the brain — or, once it has infected the brain, from progressing rapidly — appears to be to keep the HIV-infected person's immune system as strong as possible. New research suggests that HIV patients who have healthy immune systems and are on antiretroviral therapy do not develop PML.

Some experts recommend treating PML specifically by using antiretroviral drugs that cross the blood-brain barrier. These include AZT, stavudine, didanosine, zalcitidabine, lamivudine, nevirapine, and amprenavir.

Medical experts also recommend that clinicians use MRI to monitor changes in the size of PML lesions during a course of treatment.

There also is a controversial and toxic drug called cytosine arabinoside, often used as chemotherapy for leukemia and cancer, that can be used to treat PML. Clinicians administer the drug by placing a shunt into the patient's brain or vein and delivering the drug directly.

The drug's possible side effects are nausea, bone marrow toxicity, and fevers. Prednisone and granulocyte colony-stimulating factor (G-CSF) may be administered to help reduce side effects.

The other problem with cytosine arabinoside is that its results have been mixed in clinical studies. Some research has shown it to have no benefit.

Researchers also are investigating the use of cidofovir for treating PML. This drug must be injected intravenously and must be given with probenecid to reduce the risk of kidney toxicities. But the drug is still being studied and it has many side effects, so it is a long way from being of value in treating PML.

**• What are the sources of information for the material presented here?**


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