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Special Issue

- This month's entire issue is devoted to a single article profiling the care of HIV-infected refugees.

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As Population of HIV-Infected Refugees Rises, Providers Need to Give Them Special Care

HERE'S HOW RHODE ISLAND DEALT WITH CHALLENGE

By Melinda Young

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Health care providers in less populated cities and states are seeing increases in both their general immigrant populations and their HIV-infected immigrant populations.

Before 2000, HIV-infected refugees were restricted from entering the United States. But a change in policy allows them to enter on the condition that their health care is arranged, says Curt Beckwith, MD, an assistant professor, division of infectious disease, Brown Medical School and Miriam Hospital in Providence, RI.

"The reasoning was they didn't want to let in refugees who would be a burden on the U.S. health care system, but if care could be arranged a priori to their arrival, then that would be okay," Beckwith explains. "Once that policy was put into effect, then refugees with HIV began to arrive here."

While most people applying for permanent residence in the United States are subject to an HIV antibody test, certain immigrants may qualify for an HIV waiver, according to the "HIV/AIDS and Immigrants: A Manual for Service Providers," published in 2004 by the San Francisco AIDS Foundation and National Immigration Project of the National Lawyers Guild.[1]

The waiver may apply to asylees, refugees, special immigrant juveniles, and others who applied through the legalization program. Those who apply for the waiver have to meet a public charge condition in which the applicant ensures that he or she will not hinder public health and will not cost a government agency, unless the agency has given prior consent for services or benefits.[1]

With the help of health care providers and humanitarian groups, more HIV-infected refugees have legal status in the United States, and some of them are

ending up in smaller cities.

For example, many Liberian refugees and refugees from other parts of Africa have arrived in the tiny state of Rhode Island to receive care for their HIV infection, Beckwith says.

"We have a refugee population at our center of about 50 refugees—mostly from West Africa," Beckwith says. "We have a large Liberian refugee population in Providence, so we've seen a lot of Liberian refugees."

Typically the way it works is: the Providence clinic is contacted by an international institute that works with a federal refugee settlement agency, and the institute will say it has a number of HIV-infected refugees, Beckwith explains.

"We say, 'Great! We'll make appointments for them and do intakes and so forth,'" Beckwith says. "That works very well for us, although the relationship might be tougher if the numbers were higher."

So far, the clinic has incorporated about 50 refugees into its practice without a great deal of strain on resources, he adds.

The HIV-infected refugees need to have their HIV care assured prior to their departure from refugee settlement camps and organizations, Beckwith explains.

"Without care, they are not allowed to come into our country," he says. "So the refugee organization arranges for care through our clinic, and that has resulted in an influx of refugees over the past four to five years."

Although the total numbers of HIV-infected refugees moving to the United States are not large, the small population of refugees presents health care providers with many challenges, says Christine A. Kerr, MD, a clinical fellow at Beth Israel Deaconess in Boston, MA. Kerr previously worked with HIV-infected refugees when she was a chief resident at Brown University's Miriam Immunology Center.

For example, one woman who came to the United States from Liberia had lived in a refugee camp for several years, Kerr recalls.

"She had seven children, four of whom were killed in a civil war," Kerr says. "I think the other three were still in the refugee camp, and she was here by herself at great personal expense."

The woman's HIV infection was significant, but she faced a myriad of other problems that were more pertinent to her medical situation, Kerr says.

"She had a lot of depression and anxiety that were contributing to her difficulty in taking her medication while in this country," Kerr explains. "The patients we see, by and large, tend to be patients who are very committed to their medical care and follow-up, but they face significant challenges that are separate from their HIV care."

Providers working with this population need to keep both co-morbidities and psychosocial factors in mind, Kerr and Beckwith say.

"My interest has been to look at this population and say in general there are differences in the refugee population in terms of other disease processes and other co-infections," Beckwith says.

Beckwith has been researching the question of how the HIV-infected refugee population compares with the general U.S. population of HIV-infected individuals.

In the United States, HIV is transmitted because of

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three factors: injection drug use, men who have sex with men (MSM), and heterosexual activity, Beckwith says.

"In developing countries, such as in sub-Saharan Africa, that's not the case at all," he says. "It's much more of a heterosexual epidemic."

So Beckwith, Kerr, and other investigators decided to look at the risk factors for HIV among foreign-born people, as well as at which stage of disease they first presented for health care.

"We also looked at other infections with the thought that there'd be more hepatitis B and less hepatitis C among refugees than among HIV patients who were born in the United States," Beckwith says. "And they'd be more likely to have tuberculosis and parasitic infections when compared to people born in the U.S."

The findings showed that heterosexual sex was a pr mary risk factor among the immigrants, and they had relatively high CD4 counts and low levels of HIV viremia.[2]

Investigators also hypothesized that the refugee population would have higher levels of psychosocial issues than the general HIV population, but that their levels of drug abuse and severe disabling mental illness, such as schizophrenia, would be lower, Kerr says.

"By and large, that did turn out to be true," Kerr says.

Investigators found that the immigrant population had a high incidence of psychiatric co-morbidities.[2]

"The levels of drug and alcohol abuse were quite low among the refugees," she adds. "Depression and post-traumatic stress disorder [PTSD] were higher in the refugee population than what might be expected in the general HIV population in the U.S."

One of the most difficult aspects to caring for refugee populations is the cultural differences, Beckwith says.

"Our western model of medical care is something they're not familiar with, and it's hard for them to accept our model of care," he says. "So it's challenging to sit down with a refugee who just arrived in the United States and try to ex-plain what HIV infection is and what our treatment is and when we'll start treatment."

From many refugees' perspective, HIV is a disease that kills people, so their outlook on being infected is impacted by this.

"Communication can be difficult, and you have to do it in a culturally sensitive way, and it may take multiple conversations," Beckwith says.

For instance, an HIV-infected refugee might not understand why a physician would withhold treatment and say the person is doing well clinically without it, he notes.

"They think, 'I have HIV, so why wouldn't I need treatment?' and that's very hard to explain and may take multiple appointments," he says. "The international institute may need to get involved, and there could be a distrust of our medical system."

When there is an available clinical trial for HIV patients, the trust and communication barriers become even more prominent.

"Trying to explain what a clinical trial is and the benefits of the trial can be very difficult," Beckwith says. "So our enrollment of refugees in clinical trials is very low."

Here are some ways HIV clinicians can improve the care of immigrant patients:

• Check for foreign diseases: "They should be tested for parasites and have their blood checked for malaria," Kerr says.

Typical clinical care includes tuberculosis testing, chest x-ray, parasite screening, and viral hepatitis screening, Beckwith says.

"Everyone has these done upon entrance to the United States," he says.

"Providers also need these patients' vaccination records, and most of them do not have records and may not have had any vaccinations in their lifetime," Beckwith adds.

"This is a population that was forced out of their homes unexpectedly," Kerr says. "Many of these patients grew up where there was no vaccination program."

The Providence clinic staff found it very difficult to vaccinate immigrant patients, she notes.

"There were significant challenges to doing a multi-series vaccination program because it requires a bunch of visits and psychosocial issues at each visit," Kerr says. "It was challenging to providers to get all of the preventive health services done."

For one thing, finding out if the patients had any previous vaccinations was important, but difficult to ascertain, she adds.

• Assess for psychiatric illness: "Because of their traumatic experience of being a refugee and being in camps for many years before coming here, for all of our patients we make an assessment as to what other psychiatric illnesses might be present," Beckwith says. "And if they are present, we may get help through a psychiatric referral or through the international institute."

Often if there is a psychiatric illness, it will involve PTSD, and in refugee patients this disorder may be manifested differently than it manifests in people who were born in the U.S., Beckwith notes.

"It's different in terms of cultural issues and experiences, and, to be honest, I'm not sure it's adequately addressed in refugees," he says.

However, if PTSD is present then it could impact medical care, and so it has to be treated, Kerr says.

"PTSD is huge," Kerr says. "The woman who had four children who had been killed had a limp and sore leg, which was a result of when she was raped in Liberia."

• Deal with cultural/language differences: The Providence clinic used translators both in person and by telephone, Kerr says.

"The hospital had telephone translators available all the time," she says. "Language problems definitely add another layer of complexity, and it partly explains why it's so hard to get so many of these things done."

It would be helpful if HIV providers were trained about certain cultural differences among refugee/immigrant populations seen in their area, Beckwith suggests.

One way to help with the cultural barrier would be to train peer educators from the patients' same culture, he says.

Some of the cultural differences include the patients' attitudes toward stigma and conceiving children, he notes.

"We generally counsel HIV-positive patients to not get pregnant, but a lot of patients from developing countries and refugees want to get pregnant, and cultural reasons drive this desire," Beckwith says.

Beckwith's research found that the immigrant population had high rates of pregnancy.[2]

The key is to cultivate peer educators within the impacted community to help with the care and transition, he adds.

There are financial and medical insurance obstacles, as well, but HIV clinics are accustomed to dealing with these for the sake of improving both the individual patients' care and for protecting the community against further HIV infection, Beckwith says.

"This is an interesting and challenging population, but you can make real differences in their lives," Beckwith says. "These people are going through a really tough time, and HIV can be a big component of that, and so the more care you can provide for them—the better." ■

References:

1. HIV/AIDS and Immigrants: A Manual for Service Providers. San Francisco AIDS Foundation and National Immigration Project of the National Lawyers Guild. 2004 Ed.:1-59. Web site: www.nationalimmigrationproject.org.
2. Kerr C, Blood E, Aggrey G, et al. HIV-infected refugees in Rhode Island. Abstract presented at the 44th Annual Meeting of IDSA, held Oct. 12-15, 2006, in Toronto, Ontario. Abstract:922.

CME Objectives

• To present the latest data regarding the diagnosis and treatment of various travel-related diseases;

• To present new data concerning recommended precautions and prophylaxis for patients traveling to specific areas of the world; and

• To alert the readers to recent disease outbreaks and epidemics. ■

PHARMACOLOGY WATCH

Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Long-Awaited Torcetrapib Will Not Be Released, Too Risky

Torcetrapib, a cholesteryl ester transfer protein (CETP) inhibitor, has been in development by Pfizer for nearly 15 years. The drug has been shown to elevate HDL levels while reducing LDL levels, prompting hopes that torcetrapib would be the first in a new class of important cholesterol medications. In December, Pfizer abruptly pulled the plug on further development of torcetrapib when the Investigation of Lipid Level Management to Understand Its Impact in Atherosclerotic Events trial showed an increase in death from all causes associated with the drug, including an increased rate of cardiovascular events and hypertension. A new study points out a possible mechanism for the lack of cardiovascular benefit. In the international study, 1,188 patients with cardiovascular disease underwent intravascular ultrasonography. They then received atorvastatin and were randomized to receive 60 mg of torcetrapib daily or placebo along with atorvastatin for 24 months. Atorva/torcetrapib resulted in a 61% relative increase in HDL and a 20% further reduction in LDL, resulting in an average HDL higher than LDL. But the drug combination was also associated with an increase in systolic hypertension of 4.6mm Hg, and more importantly an increase in atheroma volume of 0.12%, compared to an increase of 0.19% in the atorvastatin alone group (P = 0.72). The authors conclude that treatment with the CETP torcetrapib was associated with improved lipid endpoints, but was also associated with an increase in blood pressure and no significant decline in coronary atherosclerosis (*N Engl J Med.* 2007;356:1304-1316.). In an accompanying editorial, Dr Alan Tall holds out hope that other CETP inhibitors may not show the same adverse effects but suggests that further development of this class of drugs needs to proceed with caution (*N Engl J Med*. 2007;356:1364-1366). ■

IBS-Drug Treatment Pulled, CV Side Effects

Tegaserod (Zelnorm), Novartis Pharmaceutical's drug for irritable bowel syndrome has been removed from the market by the FDA based on recent findings of increased risk of serious cardiovascular events associated with use of the drug. Tegaserod was approved in 2002 for women with irritable bowel syndrome whose primary symptom was constipation. It was given the additional indication in August 2004 for chronic constipation in men and women under the age of 65. Withdrawal was based on analysis of 29 studies involving more than 18,000 patients that showed a small, but statistically significant increase in the risk of cardiovascular side effects (0.1% serious adverse effects with tegaserod vs 0.01% with placebo). The FDA may allow continued use of the drug in a limited number patients for whom no other treatment options are available and the benefits of tegaserod outweigh the chance of serious side effects. The FDA may consider limited reintroduction of the drug at a later date if the population patients can be identified in whom the benefit of the drug outweighs the risk. ■

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. Questions and comments, call: (404) 262-5431. E-mail: jennifer.corbett@ahcmedia.com.

Drug Combo Better for Migraine Treatment

Naprosyn plus sumatriptan is better than either drug alone for the treatment of acute migraine according to a new report. In 2 studies, nearly 3,000 patients with a history of migraine were randomized to sumatriptan 85 mg plus naproxen sodium 500 mg, both drugs alone, or placebo to be used after the onset of a migraine with moderate to severe pain. The primary outcome was headache relief at 2 hours, absence of photophobia, absence of phonophobia, absence of nausea, and sustained pain-free response. Sumatriptan plus naproxen was superior to placebo in all measures and was superior to either drug alone in sustained pain-free response. The incidence of adverse effects was the same for the combination as for the individual medications. The authors conclude that sumatriptan 85 mg plus naproxen 500 mg as a single pill for acute treatment of migraine is more effective than either drug as monotherapy (*JAMA*.2007; 297:1443-1454.). Pozen Pharmaceuticals/ GlaxoSmithKline is developing the combination pill, which is expected to be approved later this year under the trade name Trexima. ■

Pergolide Off the Market, Heart Disease Risk

Pergolide (Permax) is being withdrawn from the market after reports of serious valvular heart disease associated with the drug. Pergolide is a dopamine agonist used for the treatment of Parkinson's disease, hyperprolactinemia and pituitary tumor (?). The action was prompted by 2 reports in the January 4, 2007, *New England Journal of Medicine* that showed increased rates of valvular dysfunction in Parkinson's patients who were taking the drug. These findings coupled with the availability of other dopamine agonists prompted the FDA's action. Valeant Pharmaceuticals is removing Permax brand pergolide as are all generic manufacturers. ■

Hormone Treatment, Does Timing Matter?

Further analysis of the Women's Health Initiative suggests that the timing of the initiation of hormone therapy may have an effect on the risk of cardiovascular disease. The analysis looked at postmenopausal women who had undergone a hysterectomy and were randomized to conjugated estrogen or placebo and women who had not had a hysterectomy who were randomized to conjugated estrogen plus medroxyprogesterone or placebo. The main outcomes were coronary heart disease (CHD) and stroke. Women who initiated hormone therapy within 10 years of menopause had a lower incidence of CHD (HR 0.76 [95% CI, 0.50-1.16]), which equates to 6 fewer events per 10,000 person-years. For women who initiated therapy 10-19 years after menopause the hazard ratio was 1.10 (95% CI, 0.84-1.45), and for women who initiated therapy 20 years after menopause the hazard ration was 1.28 (95% CI, 1.03-1.58) or 12 excess events per 10,000 person years. CHD risk increased when patients were stratified by age as well. Hormone therapy increased the risk of stroke with no significant difference based on time since menopause or age. There was a non-significant trend for improved overall mortality in younger women. The authors conclude that women who initiated hormone therapy closer to menopause had a reduced risk of CHD, with an increase risk among women more distant from menopause although the trends did not meet their criteria for statistical significance (*JAMA*. 2007:297;1465-1477.). ■

FDA Actions

The FDA has approved Cangene's immune globulin to prevent reinfection with the hepatitis B virus in certain liver transplant patients. The product was previously approved for preventing hepatitis B infection after exposure in 2006. It is marketed as HepaGam B.

The FDA has banned rectal suppositories that contain trimethobenzamide due to lack of efficacy in preventing nausea and vomiting. The popular suppositories have been marketed under various trade names including Tigan, Tebamide, T-Gen and others. The drug will still be available as oral and injectable preparations. The evaluation which eventually led to the withdrawal is part of the FDA's ongoing Drug Efficacy Study Implementation (DESI) which evaluates older drugs previously approved based on safety data to make sure that they are also effective.

The FDA has approved Merck's combination diabetes drug Janumet, which combines sitagliptin with metformin. Sitagliptin, which is a dipeptidyl peptidase-4 inhibitor, has been marketed by Merck since last October under the trade name "Januvia." The combination is approved for the treatment of patients with type 2 diabetes; it should be dosed twice daily with meals with gradual dose escalation. ■