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Worrisome New Link: AIDS Drugs and Leprosy

By DONALD G. McNEIL Jr.

With affordable AIDS drugs arriving in many poor countries, experts say a startling and worrisome side effect has emerged: in some patients, the treatment uncovers a hidden leprosy infection.

No one knows how widespread the problem is. Only about a dozen cases have been described in medical literature since the first one was found, in London in 2003. But AIDS specialists in Brazil, India, Africa, the Caribbean and elsewhere are reporting that some patients on life-saving antiretroviral drugs are developing painful facial ulcers or losing feeling in their fingers and toes.

And in the third world, where 300,000 new cases of leprosy were discovered last year and where 38 million are infected with the AIDS virus, the problem will inevitably get worse, experts say.

“This is just the peak of the iceberg,” said Dr. William Levis, who treats leprosy patients at Bellevue Hospital in New York City. “It’s early in the game. Most physicians don’t even think about leprosy, so there’s probably much more around than we know.”

Dr. Gilla Kaplan, a professor at the University of Medicine and Dentistry of New Jersey and one of the first to study connections between AIDS and leprosy, agreed.

Antiretroviral treatment, she said, “is going to flush out the silent leprosy by making it symptomatic.”

Because leprosy, a bacterial disease, can be treated with specialized antibiotics that are supplied free by the Novartis pharmaceutical company, there is little prospect of a worldwide epidemic or large numbers of deaths. “It’s a matter of concern for the individual patients,” said Dr. Denis Daumerie, who leads the efforts by the World Health Organization to eliminate leprosy. “It’s not a matter of concern for public health.”

Still, the disease requires taking multiple pills for six months to two years — an added burden for people who typically already take three AIDS drugs. And because the problem is little known, it often takes doctors weeks to figure out what new ill is besetting their AIDS patients.

Experts say the problem arises when the AIDS drugs cause the immune system to recover. It then generates new white blood cells that carry the bacteria from old, silent leprosy infections to the skin of the face, hands and feet.

That is a new twist on a medical paradox that has confounded tropical-disease specialists for 20 years.

In the mid-1980's, as it became clear that AIDS was not primarily a disease of gay American men but was killing millions of people — men, women and children — in poor countries, many public health doctors prophesied that it would be a double disaster for those with leprosy.

It seemed a logical assumption since leprosy is caused by a germ from the same family of waxy-walled bacteria as those that cause tuberculosis and mycobacter avium, two major killers of AIDS patients. But it proved a false alarm.

“People expected a big surge in leprosy, but it didn't happen,” said Dr. Diana N. Lockwood, a leprosy expert at the London School of Hygiene and Tropical Medicine.

When the predictions did not come true, she said, “we assumed that co-infected people just died before their leprosy became manifest.” The incubation period for the most easily diagnosed form of leprosy is 8 to 13 years, while the incubation period for AIDS is 8 to 10.

But leprosy in people known to have been already infected did not seem to worsen when those patients developed AIDS, too, showing that the two diseases can apparently coexist without reinforcing each other.

So it came as a shock to doctors when AIDS treatment caused hidden cases of leprosy to appear.

The first such patient described in a medical journal was Dr. Lockwood's, a Ugandan exile in London who was being treated for both tuberculosis and AIDS, and suddenly developed a swollen lesion on his face.

“It took us a while to realize it was leprosy,” Dr. Lockwood said. “Since then, we've seen more cases in people from Brazil and India.”

Depending on symptoms, leprosy is often initially misdiagnosed as arthritis or lupus. Painful facial lesions, which are less common, can have many causes; in the Uganda man's case, doctors said, his immune system probably formed nodules around bacteria next to a facial nerve.

Dr. Michael S. Glickman, a bacteriologist at Memorial Sloan-Kettering Cancer Center who

treated the only co-infected case known in New York, said he too had some difficulty diagnosing his patient's leprosy.

Dr. Glickman's patient, a man from Burkina Faso, was suffering from advanced AIDS when he first saw Dr. Glickman six years ago, with a CD4 cell count below 10 (normal is 500 or more). As the patient recovered on antiretroviral therapy to a CD4 count of 600, he developed a lighter-colored patch of skin. Dr. Glickman noticed that it was slightly numb to the touch. Fortunately, he had once visited Dr. Levis's clinic at Bellevue, and made the connection.

"It was so unremarkable that, if I hadn't seen leprosy patients, I wouldn't have known what it was," he said.

His patient's leprosy was eventually cured, but he had to have an unusual drug regimen because one typical leprosy drug reacts badly with the protease inhibitors taken by AIDS patients.

Treatment in cities like New York and London is relatively easy, but the real crisis, experts said, will evolve in poor countries with dual epidemics.

In French Guiana, for example, Dr. Pierre Couppié, chief of dermatology at the Central Hospital in Cayenne, said he believed that about 1 in every 500 AIDS patients would develop leprosy lesions soon after starting treatment.

Brazil has the world's highest per-capita leprosy rate and also one of the most effective AIDS treatment programs in the developing world, and seven Brazilian cases have been mentioned in medical literature. No countrywide study has been done, but Dr. Patricia D. Deps, a leprosy expert at the Federal University of Espirito Santo in Brazil, said it was "becoming more and more common."

"We don't have good numbers, but we think about 2 percent of the leprosy cases in Brazil are co-infected with H.I.V.," Dr. Deps said. The country that most worries experts is India. Not long ago, it had 70 percent of the world's leprosy cases. Its official caseload is a bit of a mystery now. After an aggressive 20-year campaign to find and treat new cases, India officially declared leprosy "eliminated as a public health issue" last year. However, that statement was carefully crafted: it means there is a national average of lower than 1 case per 10,000 citizens, which could be as many as 100,000 new cases a year.

At the same time, with about 5.2 million people infected with the AIDS virus, India is poised to outstrip South Africa as the country with the most AIDS victims. But its epidemic began much later than South Africa's or Brazil's, and it has been slow to roll out AIDS treatment. As treatment grows, leprosy may surge along with it.

Other countries with high numbers of leprosy victims are Myanmar, Madagascar, Nepal and Mozambique.

But there are also great unknowns. “It depends on how good the medical system is,” Dr. Lockwood said. “For example, last year, Congo discovered 11,000 new cases.”

Novartis provides the W.H.O. with clofazimine, rifampicin and dapsone, the standard leprosy regimen, in blister packs and boxes so patients can be handed six months of treatment at a time, already divided into daily doses.

But treating leprosy in AIDS patients may turn out to be more difficult, doctors say, because rifampicin cannot be used. And treatment in wealthy countries includes more expensive anti-inflammatories, as well as thalidomide, which blocks a common inflammatory complication.

Because thalidomide causes severe birth defects, the World Health Organization opposes its use in the third world.

Doctors have long known that dormant diseases can surge as a weak immune system recovers. The threat is sometimes called “Haart attacks” — a grim pun on the medical acronym for “highly active antiretroviral therapy.”

The recovering immune system regains its ability to create fevers, flood infected tissue with white blood cells, break bacteria down into toxic waste products and build nodules around bacteria it cannot kill.

But in a weakened patient, that inflammatory response itself can be dangerous. For example, when doctors know that an AIDS patient has tuberculosis, they often try to give TB drugs for two months to suppress the bacteria before starting antiretrovirals, because the patient’s own immune attack on the tuberculosis bacteria in the lungs can be fatal.

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