The War on Cancer

With AIDS-defining illnesses fading increasingly into the wings, a new health challenge for people living with HIV has moved toward center stage.

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As the HIV population ages and confronts health challenges that members of the general population naturally experience in their graying years, a new front in the battle against the virus has opened. What was once a conflict against AIDS-defining opportunistic infections has increasingly become a war on “non-AIDS-defining cancers” (NADCs). People living with HIV, it has become clear in recent years, are at markedly higher risk for a wide array of malignancies and tend to experience them at much younger ages than those without the virus.

While scientists are only just beginning to tease apart the myriad variables that may contribute to the appearance of these cancers—smoking, drug use, hepatitis B or C coinfection, an immune system damaged by HIV, cellular inflammation as a reaction to the virus—one thing is clear: Greater vigilance is needed to better identify these cancers in earlier stages in order to best care for people with HIV and ensure their survival. Because the good news is, this increased risk of cancer notwithstanding, recent research suggests that people with well-cared-for HIV may expect to live a normal life span.

“The [cancer] rates are higher in HIV patients, but it’s not that everyone with HIV will get one of these cancers,” says John F. Deeken, MD, a medical oncologist at Georgetown University Medical Center. “It’s just that the rates compared to the general population are higher, which argues for us to try to be more aggressive, to figure out why and how to prevent it, and certainly how to treat it if they do.”

Deeken is the lead author of a literature review recently published in Clinical Infectious Diseases (CID) that spells out in stark terms just how broad the new cancer epidemic is among people with HIV. While research studies have failed to comprehend exactly why, they have illuminated that there are increased risks for lung, liver, kidney, anus, head and neck, and skin cancers, in addition to Hodgkin’s lymphoma.

The paper cites numerous studies showing that AIDS-defining cancers like non-Hodgkin’s lymphoma, KS and cervical cancer declined three-fold between 1995 and 2005, while NADCs tripled during the same span. People with HIV are nearly three times as likely as the general population to experience an NADC. The risk of anal cancer is at least 33-fold higher, Hodgkin’s

lymphoma 15- to 30-fold and liver cancer 7-fold higher.

The research so far has suggested that, at least in the United States, increased risk of NADCs is found only among white males living with HIV, with no apparent increases in women or other ethnicities. However, this projection may be skewed by lack of reporting for minorities.

The greatest risk factor for developing NADCs is simply getting older: the risk for those greater than 40 years of age is 12 times that of the general population.

The research about potential causes for all these increases is in its infancy, but multiple theories abound and investigators are beginning to bring clarity that may soon aid in prevention efforts. HIV itself appears to cause changes in human cells that make them more susceptible to cancer. Also, there is a high prevalence of coinfection with other cancer-causing viruses in the HIV population, such as hepatitis B or C (HBV/HCV), human papillomavirus (HPV) and the Epstein-Barr virus (EBV). People with HIV tend to have a faster progression of liver disease from hep B and C. And while EBV causes about a fifth to a half of cases of Hodgkin's disease in the non-HIV-infected population, an estimated three-quarters to 100 percent of the disease is associated with EBV in people with HIV.

Thus far, there has been conflicting research as to whether antiretrovirals themselves have a positive, negative or no effect on cancer rates.

Deeken's paper cites research showing that cancer screening is actually conducted less frequently in HIV-positive people than in the general population. He advises people living with the virus to undergo the regular screens for cancer, such as mammograms and colonoscopies, and to talk to their doctor about possibly receiving the screens at an earlier age—having a colonoscopy at 40 rather than 50, for example—especially if there are other risk factors or a family history of cancer. His paper also advises that treatment for hepatitis B or C coinfection is vital for preserving liver health, and that the new vaccine against HPV (the virus can cause anal cancer) should be used in men rather than just women, as the FDA currently advises.

Lung Cancer: the Biggest Threat

One out of three cancer deaths and 10 percent of all deaths among people with HIV are a result of lung cancer. What's more, people with HIV are at three times greater risk for lung cancer, and they experience an onset of the disease 25 to 30 years earlier than the general population. A recent commentary published in CHEST Journal finds that, despite the fact that lung cancer is the most prevalent NADC, clinicians have only limited recognition of this insidious threat.

The paper finds that, on average, people with HIV who are diagnosed with lung cancer are between 38 and 57 years old, compared with 70 years old for the general population. Even more troubling is the fact that more than 80 percent of cases are identified in stages III or IV (to quote the Pulitzer Prize–winning play Wit, "There is no stage V"). There is also apparently an exponentially increased risk for developing the disease as people age, with the risk relative to the

general population increasing from double for people in their 30s to 7-fold in their 40s, 14-fold in their 50s and 28-fold above the age of 60.

Cigarettes are a major culprit, considering that 60 to 80 percent of people with HIV are smokers. However, research increasingly suggests that more than just tobacco is to blame. HIV on its own appears to about double the risk of lung cancer. While there is conflicting evidence on the subject, immunosuppression may play a factor in this increased risk, suggesting that higher CD4 counts may lower the chances of developing lung cancer. Chronic inflammation from infections or other diseases, as well as recurring pneumonia, may also be linked to lung cancer.

“Awareness is a big problem,” says Don Sin, MD, MPH, a chest physician and a professor of medicine at the University of British Columbia, who is one of the study’s authors. “I don’t think the general practitioners or even specialists in HIV care are really plugged into this high risk of cancer in the HIV population. They say, ‘You have HIV, we’d better treat you for viral load, CD4 counts, make sure you don’t get opportunistic infections. We should monitor you for cardiovascular disease, diabetes.’ But rarely does lung cancer come up in the conversation.”

According to Sin, the upside is that there are greater tools today, including medications, to help people quit smoking. Quitting cigarettes can reduce people with HIV’s risk of dying of cancer by more than 50 percent. He advises clinicians to help HIV patients with smoking cessation and to screen for lung cancer with chest X-rays and CT scans if necessary, in order to catch the disease at an earlier stage and increase the chances of survival.

Skin Cancer: Be on the Lookout

According to another paper, recently published in the Journal of the National Cancer Institute, the HIV population is also at increased risk for non-melanoma skin cancers. Basal cell carcinomas (BCC) are twice as common and squamous cell carcinomas (SCC) are 2.6 times as common as compared with people uninfected with the virus. The good news is that, while some non-melanomas can spread to other parts of the body, most are easily cured with early detection.

Michael J. Silverberg, PhD, MPH, a research scientist at Kaiser Permanente in Oakland, California, is the lead author of the study, which was facilitated by Kaiser’s vast electronic records system. His research on skin cancers showed that the fewer CD4 cells someone with HIV has the greater his or her risk of SCCs, and the more robust the immune cells the closer the risk is to the general population’s. While he is reluctant to give a full endorsement to early treatment for HIV, he says his and other recent research “is adding to the body of evidence” supporting the apparent benefits.

“These kinds of studies are important because they point out that early therapy has important effects beyond just HIV,” Silverberg argues, “but also cancer and maybe cardiovascular disease and other conditions that are associated with aging. And these all counteract the harms of starting lifelong therapy and any adverse events related to that.”

Given these higher risk factors, Silverberg suggests that limiting excessive sun exposure may be even more important for people with HIV. He also advises regular check-ups with dermatologist to screen for abnormal moles that may be a sign of cancer. An HIV doctor should also be able to conduct this exam, but people may need to ask for one. (For information on how to identify abnormal moles, click here.)

Statins: Ammunition Against More than Cholesterol?

One arena of hope in the war on NADCs is in a class of medication many people with HIV take already: cholesterol-lowering statins. A paper published online in Clinical Infectious Diseases recently identified that statins were associated with a 57 percent reduction in the risk of developing NADCs.

“Many cancers have some component of inflammation contributing,” says the study’s principal investigator, E. Turner Overton, MD, an associate professor in the division of infectious diseases at the University of Alabama at Birmingham, alluding to the inflammation HIV causes in many human cells throughout the body. “So it kind of makes sense: If you have an effective therapy to reduce inflammation, particularly if it’s a long-term process, which is what it is with many cancers, then if you can reduce that [inflammation] over a long period of time, you might see some benefit.”

Overton feels the medical field is gearing toward a day when statins or some other inflammatory agent may become a more standard adjunct to antiretroviral therapy in order to help reduce the risk of cancers caused by long-term cellular inflammation.

In the meantime, Deeken advises people with HIV, their care givers and researchers alike to draw their swords and fight NADCs.

“This is just another challenge we’ve got to take on meaningfully as people live longer with their HIV disease,” he says, “because cancer is oftentimes a disease of the aging, so this is going to be a growing issue in the years ahead. We want to stay on top and hopefully turn this around too.”

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