HIV and Your Overall Health

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As people with HIV live longer thanks to effective antiretroviral treatment—nearly half are now 50 or older—they are prone to a host of additional health problems, known as comorbidities.

Common comorbidities among people with HIV include cardiovascular disease, diabetes and other metabolic conditions, liver and kidney problems, chronic lung disease, non–AIDS-related cancers, neurological conditions and frailty. HIV can also have a detrimental affect on mental health (see "Your Mental Health").

People who have been living with HIV for many years—especially those who have experienced advanced immune suppression and those who have taken many antiretroviral medications—are at greater risk for comorbidities. But these conditions also affect people with well-controlled HIV.

Some of these problems are associated with normal aging, but studies show that HIV-positive people tend to develop age-related conditions as much as a decade earlier than their HIV-negative counterparts.

"There's evidence that cardiovascular disease is more advanced in HIV patients—some estimates have said five to 10 years more advanced," says Steven Grinspoon, MD, a professor of medicine at Harvard Medical School and director of the Nutrition Obesity Research Center at Harvard. "Frailty is associated with senescence and may increase vulnerability to aging-related processes, and reductions in physical function suggestive of early frailty seem to be very common in HIV patients."

Frailty is characterized by muscle and bone loss, weakness and decreased energy, and it can lead to reduced strength and endurance, heightened risk of fractures and progressive difficulty carrying out activities of daily life.

HIV and Inflammation

Chronic immune activation and inflammation appear to be a common thread tying together the various coexisting conditions seen in people living with HIV.

Even in people with sustained viral suppression and a near-normal CD4 T-cell count, chronic HIV infection triggers ongoing immune activation and persistent inflammation, which can take its toll throughout the body.

“Even among patients with clinically well-controlled HIV, persistent virus in T-cell and macrophage reservoirs may lead to low-grade immune activation. Chronic immune activation may be associated with more generalized inflammation as well,” Grinspoon says. “Immune activation and inflammation may be appropriate mechanisms by which the immune system targets HIV, but these processes may cause collateral damage in multiple organs.”

Persistently activated immune cells, including macrophages and monocytes, produce inflammatory cytokines, which can alter metabolism and blood vessel function and play a role in feedback loops that further increase inflammation.

Several comorbidities commonly seen in people with HIV are associated with metabolic syndrome, a cluster of conditions—insulin resistance, abnormal blood lipid levels (dyslipidemia), high blood pressure (hypertension) and abdominal obesity—that raise the risk for cardiovascular disease and diabetes.

What’s more, some HIV-positive people develop a form of abdominal fat accumulation known as lipohypertrophy, which involves the buildup of visceral fat inside the abdomen surrounding the internal organs. This fat is metabolically active tissue that produces cytokines and hormones of its own.

“With central fat accumulation, you can get inflammatory cells like macrophages that reside in the fat and release excess cytokines, which can draw in further monocytes and macrophages that produce substances that cause insulin resistance and dyslipidemia,” Grinspoon explains. “So the inflammation begets metabolic problems, and those metabolic problems beget further inflammation. These processes are intimately intertwined.”

Conversely, although much less common in the age of effective antiretroviral treatment, some people with HIV may still develop wasting, which involved the unintentional loss of both fat and lean body mass (see “What About Wasting?”).

Heart, Liver and Kidney Disease

Numerous studies over the course of the epidemic have shown that people with HIV have a 50% to 100% greater risk of developing cardiovascular disease and its complications, including heart attacks and strokes.

Over time, plaque—a combination of fat, cholesterol, calcium and immune cells—can build up on artery walls, a process known as atherosclerosis or “hardening of the arteries.” This narrows the vessels and restricts the flow of blood. Research suggests that plaque buildup happens at younger ages in people with HIV.

What's more, bits of plaque can break off and lodge as clots in the coronary arteries that supply the heart muscle, leading to a heart attack, or in small blood vessels in the brain, causing a stroke. Plaque associated with ongoing inflammation appears especially prone to rupture, according to Grinspoon.

Inflammation can also wreak havoc on the liver. As antiretroviral treatment has dramatically reduced AIDS-related mortality, liver disease has become a leading cause of death for people living with HIV. Now that hepatitis B can be prevented with a vaccine and hepatitis C can be easily cured, fatty liver disease is becoming a major driver of advanced liver disease in HIV-positive and HIV-negative people alike.

"Fatty liver disease goes along with obesity and excess weight, and it is also seen among those with diabetes and insulin resistance, as well as those with poor diet," says Grinspoon.

Chronic hepatitis B or C, fatty liver disease, heavy alcohol use and other causes of liver injury can trigger liver inflammation followed by fibrosis, or the buildup of scar tissue, as the organ tries to repair itself. Over years or decades, this can lead to serious complications, including cirrhosis, liver cancer and the need for a liver transplant. Studies have shown that this process seems to occur faster in people with HIV.

The kidneys, too, are vulnerable to the effects of inflammation. HIV-positive people have a higher rate of chronic kidney disease than their HIV-negative peers, with African Americans having the greatest risk. Certain antiretroviral medications—in particular the older form of tenofovir—can cause kidney problems in susceptible individuals. But even people who don't use this drug have a higher likelihood of impaired kidney function. Diabetes and high blood pressure, two components of metabolic syndrome, are the leading causes of kidney disease; hepatitis C coinfection also raises the risk.

Optimizing Overall Health

Regardless of which comorbidities you may have, maintaining a healthy lifestyle is key to optimizing your overall health.

Beyond HIV and the resulting inflammation, traditional risk factors—including smoking, high cholesterol, obesity and family history—are major contributors to elevated rates of heart disease and other comorbidities among people living with HIV. One study found that such traditional factors account for about a quarter of the excess risk of cardiovascular disease in this population.

Fortunately, many of these risk factors are under your control. Smoking, in particular, substantially raises the risk of heart disease, chronic lung disease and several types of cancer.

"I want to emphasize that traditional risk factors matter," says Grinspoon. "Stopping smoking is the number one most important thing you can do. It's really important because smoking may interact with inflammation and cause particularly severe disease."

Grinspoon is the principal investigator for a large trial called REPRIEVE that aims to learn more about cardiovascular disease among people living with HIV. The primary goal is to see whether a statin medication can prevent heart disease in this population. Statins not only lower cholesterol but also have anti-inflammatory properties, so they may offer a two-for-one benefit for people with HIV. Sub-studies will look at the effects of the statin on frailty and kidney function.

With 7,700 participants from 12 countries, REPRIEVE also has the potential to shed light on many other questions about the health of people living, and aging, with HIV. The study is now fully enrolled, and the primary results are expected in 2023.

In the meantime, to minimize the risk of heart disease, liver disease and other comorbidities, Grinspoon recommends a healthy diet, weight management, exercise and using medications to control hypertension, blood glucose and lipids. He suggests a balanced diet that includes polyunsaturated fats—for example a Mediterranean diet—and one that is low in salt and fructose, as "fructose contributes significantly to fatty liver disease."

"Exercise is important in two ways," he continues. "One, it helps reduce weight, and two, it's anti-inflammatory. It will help your blood pressure and help your glucose. Getting some exercise every day would be great."

Last but not least, it's essential to start or stay on effective antiretroviral therapy to keep viral load—and the resulting inflammation—as low as possible, he advises. "I think that's the state of the art right now."

Tips for Your Overall Health

- Quit smoking
- Limit alcohol and drug use
- Eat a healthy diet
- Get enough exercise
- Get adequate sleep
- Find ways to reduce stress

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