The changing picture of HIV

In the mid-to-late 1970s, a small but growing number of relatively young men and women sought care at leading hospitals in Brussels, Cologne, Kinshasa, New York, Oslo, Port-au-Prince, Paris and San Francisco. They were experiencing many of the following symptoms:

- persistently swollen lymph nodes
- fever
- unintentional weight loss
- fatigue
- repeated episodes of diarrhea
- an increasing number of skin lesions
- oral yeast infection (thrush)

The results of blood and other tests suggested that their immune systems were very weak. Subsequently, they all developed life-threatening infections and unusual cancers. Doctors were baffled that previously healthy young people would develop such a strange collection of symptoms and infections. We now call this AIDS.

By 1983, the mystery was partly solved when French scientists found the germ responsible for AIDS from samples of a patient’s lymph nodes. We now call this HIV.

Tales of simplicity

Understanding exactly how HIV causes AIDS has proven elusive, even in the present era. Initial theories based on limited evidence suggested that HIV attacked a key cell of the immune system—CD4+ T-cells (or simply, CD4+ cells). Researchers thought that by wiping out these cells HIV paved the way for immune deficiency.

The splendor of complexity

However, with the passage of time it has become clear that HIV does more than attack CD4+ T-cells. This virus also infects several other types of immune cells, such as dendritic cells (which help to amplify the immune response) and macrophages (which help to alert the immune system to invading germs and also attack those same germs and tumours). HIV-infected cells also spew out a range of proteins that confuse and increasingly disable the immune system, perhaps even turning this vital defense system against itself.

Emerging research suggests that HIV infection results in an additional problem—one that can affect many organs/systems—called inflammation.

A virus’ touch

It seems that from as early on as the point of first contact—when HIV invades the wet tissue of the anus, penis or vagina—it begins the process of causing deep and lasting changes to the immune system. Increasingly, researchers are realizing that HIV infection triggers the release of high levels of chemical signals that put the immune system into a state of permanent activation. Over the short-term, this activation is generally helpful when mobilizing the immune system against invading germs. However, in the case of HIV, activation helps the virus infect cells.

Prolonged immune activation also has other unintended consequences: It reduces the life-span of vital T-cells and possibly other immune system cells. Beyond the immune system, inflammation, along with exposure to harmful proteins made by HIV-infected cells, probably does the following:

- weakens the kidneys
• accelerates liver injury caused by hepatitis B and C viruses
• damages and inflames blood vessels and hastens the onset of heart disease
• undermines the health of bones, causing them to become thinner

These are just some of the effects of continuous inflammation in the setting of long-term HIV infection. As scientists conduct further research, it is possible that there are other complications as well.

The role of therapy

In high-income countries, highly active antiretroviral therapy (HAART) is widely available. Combination anti-HIV therapy has greatly reduced deaths from AIDS-related infections and has greatly prolonged survival, at least in people who are engaged in their care and treatment.

HAART works by reducing the production of HIV. In turn, lower levels of HIV allow the immune system to begin repairing itself. Since it suppresses HIV levels, an added benefit of HAART is that inflammation is also reduced. But because HAART does not eliminate inflammation, this problem persists. Researchers are now trying to understand the roots of this inflammation and how to suppress it.

Lurking in the shadows

One possibility is that even in HAART users whose virus levels in the blood are so low that they cannot accurately be counted (so-called undetectable levels) HIV is slowly infecting immune cells deep inside lymph tissues or perhaps places where HAART cannot concentrate—the brain and spinal cord, ovaries and testicles.

Another possible cause of inflammation is this: In an attempt to rid the body of HIV-infected cells, the immune system inadvertently turns against itself, attacking immune cells and trying to reduce the hyper-activation by suppressing its own activity.

Whatever the cause of the continuing inflammation, research teams in North America and Western Europe are studying HIV infection and inflammation and trying to find ways of dampening inflammation without harming the immune system.

There are many compounds that have anti-inflammatory activity, including the following:
• aspirin or related compounds
• fish oil
• statins – this is the name given to a group of cholesterol-lowering medications, such as atorvastatin (Lipitor) and rosuvastatin (Crestor)
• drugs used to treat arthritis and other inflammatory conditions

Researchers now have to perform lab experiments using HIV-infected cells, monkeys infected with the AIDS-causing simian immunodeficiency virus (SIV) and the above-listed or other compounds. Such experiments are necessary, as some anti-inflammatory compounds can severely weaken the immune system (excessive doses of aspirin or fish oil can cause bleeding, and so on).

In this issue of TreatmentUpdate, we report on several developments in the field of inflammation and HIV.

REFERENCES:


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Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.