Starting therapy—looking back

In the mid-1990s, highly active antiretroviral therapy (HAART) was introduced in high-income countries and its impact on the AIDS pandemic was striking. For the first time in the history of AIDS, people experienced sustained recoveries from life-threatening infections and cancers.

The reason for these favourable changes became apparent in lab test results from people taking HAART. These tests showed that HIV levels in the blood fell to very low levels in people who could adhere to and tolerate therapy. Also, because of HAART, for the first time in the epidemic the immune system experienced prolonged healing as T-cell counts rose, sometimes dramatically.

Not surprisingly, treatment guidelines were swayed by these changes and began to encourage the use of HAART relatively early in the course of HIV disease.

However, shortly after 1996, despite the stories of near-miraculous recovery from AIDS, it was clear that HAART had some drawbacks, including the following:

- A handful of pills needed to be taken several times daily, sometimes with demanding food and water restrictions.
- Some pills had to be taken on a strict every-eight-hour schedule.
- Certain drugs, such as ritonavir (Norvir), were initially prescribed at doses far higher than those used today, which could lead to unpleasant side effects such as intense nausea and diarrhea.
- Drug combinations used at the time, such as d4T (Zerit, stavudine) and ddI (didanosine, Videx), could lead to painful nerve damage in the hands and feet (peripheral neuropathy).

As the euphoria of HAART’s arrival faded, the side effects and toxicities of some of the older drugs became apparent. The strange and disturbing collection of symptoms called the HIV lipodystrophy syndrome appeared as the body shape of some HAART users changed due to a combination of fat build-up in some body parts (especially the belly) and the loss of fat in the limbs and face. The use of d4T was eventually linked to the fat loss problem, also called fat wasting or lipoatrophy.

By 2001, many factors—such as the inconvenience of medication-taking, the burden of adherence, side effects and new knowledge about how HIV damaged the body—coalesced and resulted in the following:

- research on supervised interruption of treatment began
- treatment guidelines encouraged delaying therapy until the immune system deteriorated to near-critical levels; in practical terms, some patients would then delay starting therapy for as long as possible

In this issue of TreatmentUpdate, we highlight two issues of importance to many patients and their care providers—recent changes to treatment guidelines in high-income countries and the impact of treatment interruptions.
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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

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