Cure research takes off

It has been 32 years since AIDS was first recognized and 30 years since the cause—a virus we now call HIV—was first isolated. In that time enormous advances have been made: There are tests that can detect HIV and treatment (commonly called ART or HAART) has transformed HIV into a chronic illness. Furthermore, the power of ART is so profound that a young HIV-positive adult who begins treatment shortly after diagnosis today, who takes his/her medicines every day exactly as directed and who has no or limited co-existing health conditions is expected to live for several decades.

Although ART has helped to transform HIV into a chronic illness—particularly in high-income countries such as Canada, Australia and the U.S. and regions such as Western Europe—there are still issues. This treatment must be taken at least once a day, every day, for the rest of a person’s life. Such high levels of adherence may be difficult to sustain for many years. Furthermore, medicines to treat HIV, particularly the newest and most tolerable drugs, are relatively expensive. As the vast majority of HIV-positive people live in low- and middle-income countries, some researchers have wondered whether it is possible to provide care and treatment for all HIV-positive people in those places. At present, not every HIV-positive person in those countries can access care and treatment. Thus, a cure would be very desirable for many reasons.

Know your co-receptors

HIV needs at least two receptors to enter and infect a cell. The first receptor is CD4+, which is found on many immune system cells. HIV usually then needs one of two other co-receptors, either CCR5 or CXCR4.

Some strains of HIV prefer to use CCR5, others CXCR4, and still others use both co-receptors.

Back to the cure

Since the late 1980s, researchers have attempted to cure HIV infection. However, in the first two decades of the AIDS epidemic, such efforts were largely dangerous and unsuccessful.

Then, in 2008, a major development occurred. Doctors in Berlin appeared to have cured an HIV-positive man, who was suffering from leukemia, of both cancer and HIV. The “Berlin patient” had been taking ART for several years prior to his cancer treatment and received chemotherapy, radiation and transplants of stem cells. What was unique in this case was that the donor of the stem cells had a rare mutation (called a delta-32 mutation by researchers) that resulted in his cells having no CCR5 co-receptors. This made the cells somewhat resistant to HIV infection. After intensive chemotherapy and radiation, ART was withheld and the stem cells were transplanted and took hold in his bone marrow, helping to create his new immune system. However, the man’s new immune system attacked parts of his body, a complication called GvHD (graft vs. host disease), and doctors had to prescribe a mix of powerful immune-suppressing drugs to manage this complication. His cancer returned and he had to undergo intensive chemotherapy again as well as another stem cell transplant.

The Berlin patient survived all of these interventions and recurrent cancer. He has not needed to resume ART and sophisticated tests have revealed that either he has no HIV or he has extremely low levels of this virus deep within his body from time to time.

Why the cure?

Researchers are divided about why the Berlin patient was apparently cured. Research teams have proposed different possible reasons for his apparent cure, as follows:

- the intensive bouts of chemotherapy and radiation
the bone marrow transplant from a donor with a delta-32 mutation
the intensive stimulation of his immune system arising from GvHD
the use of transplant medicines, which dampen inflammation and reduce HIV's ability to infect cells

It is likely that more than one of these factors played a role in his recovery from HIV.

Excitement

The apparent cure of the Berlin patient has excited the imaginations of many researchers and doctors around the world. Clinical trials are underway, mostly in the U.S and Western Europe, assessing different methods for attempting to cure HIV infection. Eventually some of these trials will occur in Canada.

Caution needed

Some of the attempts at a cure, such as genetic therapy, have been relatively safe. However, in attempting to replicate the success of the Berlin patient, other HIV-positive people have died. This is not surprising, as intense chemotherapy and radiation with or without transplant drugs are very debilitating.

Researchers at Harvard University have attempted a variation of the protocol used with the Berlin patient. Although two HIV-positive patients with cancer have volunteered for this experiment and have survived for several years, they remain weak, both physically and immunologically. A major difference between these patients and the Berlin patient is that they have not stopped taking ART. Due to their poor state of health, their doctors have been reluctant to withhold ART, so it is not yet clear if they have been cured.

These experiments with stem cell transplants and chemotherapy and subsequent transplant drugs are dangerous and will not be done on a large scale because among HIV-negative cancer patients such procedures carry a death rate of about 15%. No one is certain about the death rate for HIV-positive people, but it is likely to be at least as high.

Much caution with intense monitoring and hospitalizations will be needed for attempts at a cure. This will particularly be the case as researchers use multiple methods on the same person to attempt a cure.

Still, researchers should be praised for showing imagination and embracing cure research. Such encouragement is necessary because many of the complex ways that HIV interacts with the immune system are not fully understood. Therefore, much research on monkeys infected with SIV (simian immunodeficiency virus), mice transplanted with human immune systems, and HIV-positive people will be needed to gain such an understanding.

The journey toward a cure will not be easy and many challenges lie ahead. Some of the challenges are known, others may only become known as experiments proceed. As with any great scientific endeavour, there will be setbacks. This means that research funding agencies and the public need to be patient. The initial wave of cure research experiments over the next five years should be viewed as exploratory and their results preliminary. This research will seek to answer important scientific questions that can then be used to build a foundation as researchers work toward a cure.

To assist researchers in developing new ideas for cure research, Canada’s premier scientific agency, the Canadian Institutes for Health Research (CIHR), will be seeking proposals from research teams across the country. These proposals will be reviewed by scientists and the most promising proposal(s) funded for five years.

Resources

Hints of a cure—the future of stem cell transplants and HIV – CATIE News
Gene therapy for HIV—outcomes from a recent experiment – CATIE News
Attempts at a cure – TreatmentUpdate

REFERENCES:


Disclaimer

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