nature medicine

20 years of HIV science

Over 20 million dead, 42 million more infected, 15,000 newly infected each day, average life span in some countries reduced from 63 to 36 years, more than 14 million children orphaned. The stark reality of the AIDS pandemic 20 years after its causative agent was first recognized is chilling. Even as these statistics become familiar they still hold the power to shock, and we should never lose sight of the staggering burden that HIV places on many populations of the world.

On 4 February 1983, scientists got their first glimpse of the virus that was to cause this modern plague. To commemorate the twentieth anniversary of that discovery of HIV-1, *Nature Medicine* has commissioned a series of commentary and review articles that look back on the milestone achievements of the past 20 years and present some of the key questions that need to be addressed in the immediate future. This special issue is timed to coincide with the upcoming International AIDS Society Conference on HIV Pathogenesis and Treatment, which will be held in Paris on 13–16 July 2003, and in particular a plenary session to commemorate the 20-year landmark.

Without a doubt, scientific progress in these first 20 years has been impressive. The commentary and review articles in this special issue capture just how far we have come and convey the state of the fields of virology and immunology at the start of the pandemic. In our opening commentary, Fauci neatly summarizes some of the high points, including blood tests and early improvements in diagnosis that directly stemmed from the discovery of HIV. That discovery process is brought to life in personal recollections from Barré-Sinoussi and then Dauguet, the first person ever to see the virus. Their articles impart the painstaking labor and collaborative efforts that fuel research progress, but also the thrill of scientific discovery.

The greatest practical successes in the fight against HIV/AIDS have been twofold: in the clinical treatment of AIDS and in the implementation of policies and strategies to prevent HIV infection. As pointed out by Pomerantz and Horn, where antiretroviral therapy is accessible AIDS has been transformed from a terrible death sentence to a chronic and, to some degree, manageable disease; in the early 1980s, life expectancy after AIDS diagnosis could be measured in agonizing months. New therapeutics aimed at novel targets in the virus lifecycle are emerging, and prospects are good that disease management will continue to improve for the fortunate few.

Prevention measures have yielded some encouraging results, and countries that have adopted progressive attitudes (open discussion and education) have made for heartening success stories. Valdiserri, Ogden and McCray describe the progress in such strategies. Through education to modify behavior, the diagnosis and treatment of other sexually transmitted infections that increase susceptibility to HIV infection and its transmission, and the use of antiretroviral drugs to prevent perinatal transmission, prevention efforts can be very effective. The development of inexpensive microbicides with efficacy against HIV promises to further bolster future prevention strategies.

Stevenson, and then Letvin and Walker, review advances in our understanding of HIV infection, from molecular through cellular and then on to systemic pathogenesis. They point out that there is much to be learned before we fully understand the molecular host-virus interactions and immune correlates of protection from disease that will inform future drug discovery and vaccine efforts.

Pope and Haase evaluate our current understanding of transmission and acute infection, from initial infection to dissemination and establishment of persistence. They emphasize that the very earliest events after infection are crucial, and there may be a significant window of opportunity that can be exploited by a vaccine-enhanced immune response.

What can we hope for from HIV vaccines? Will sterilizing immunity be attainable, or will the best we can expect merely be therapeutic, a vaccine that can bolster existing immune responses to keep up with the virus? McMichael and Hanke round up early attempts to bolster the failing immune response and the principles underlying those efforts, then bring us up to date with the accelerating pace of AIDS vaccine research. True to traditional vaccinology, we are tentatively beginning a new phase of empiricism in vaccine trials, with ever more modalities being tested in humans. A vital challenge now is how to induce a neutralizing antibody response that can augment the encouraging cellular responses induced by current vaccines. Crucially, an effective vaccine holds the promise of accessibility for all.

In our closing commentary, Weiss looks to the future and speculates on some aspects of the pandemic. He brings up the interdependency of all scientific research, how advances in one discipline continually feed another, and reminds us that uncovering fundamental principles through curiosity-driven basic research often brings serendipitous progress in unexpected areas.

So as we look back on the first 20 years of HIV science, we can reflect upon the achievements but must remember how far there remains to go. Science still does not have all the answers, and the ones it has are not equitably implemented. As with all scientific progress, advances in knowledge and technology will require political implementation if they are to benefit society at large. The current disparity in access to effective antiretroviral therapy is shameful, and science must accept its part in advocating change. Let's hope the next 20 years can redress the inequities.