AIDS: The Final Chapter?

Mathilde Krim and Rowena Johnston

WHEN THE FIRST REPORT of what came to be known as “AIDS” was published in the *Morbidity and Mortality Weekly Report* of June 1981, few could have predicted the devastation the disease would wreak. What became clear in the ensuing months, however, was the urgent need for a venue for publishing research findings that would help scientists grapple with the mysterious new killer.

In 1983 we saw the founding of the AIDS Medical Foundation (which later became amfAR) and that of *AIDS Research and Human Retroviruses*, the first journal dedicated solely to AIDS research. Together, they began to fill the gaping holes in our knowledge of a disease in which many researchers and even some physicians refused to be involved.

The need, however, was great. By the end of 1983, 4,661 AIDS cases had been reported in the United States alone. By 1993, that number had risen to 414,792, and to 908,765 by 2003. The latest data from the Centers for Disease Control (CDC) indicate that almost 1.2 million AIDS cases have been reported in the United States. By the year 2000, more Americans had died of AIDS-related causes than had died in combat during the entire twentieth century.

Now, 30 years after the launching of *AIDS Research and Human Retroviruses*, it is awe-inspiring to consider how much has been learned. Today, a person diagnosed and treated in their 20s may reasonably expect a lifespan that rivals that of his or her uninfected counterparts. Such an outcome was unimaginable in the early days of this journal, and is due largely to the advent of highly active antiretroviral therapy.

The current state of knowledge on the first class of HIV drugs, the reverse transcriptase inhibitors, was reviewed by Eric de Clercq in 1992,¹ the same year Christine Debouck² described the potential of protease inhibitors as another means of treating HIV infection. Just a year later, with funding from amfAR, Carl Wild *et al.* described for the first time the peptide that would later become Fuzeon.³ Since those early days, HIV treatment has become more complex and nuanced. The journal continues to serve the AIDS research community by publishing articles describing those challenges—such as toxicities, comorbidities, and resistance mutations.^{4–8}

Today, we find ourselves at a critical juncture. Before us stands the opportunity to end an epidemic that has taken the lives of 36 million people around the world, and continues to affect the lives of tens of millions more. To bring an end to

AIDS, we need effective means to prevent HIV transmission and a cure for those who are already infected.

Although the first reported cure of HIV⁹—only 4 years ago—served as the first impetus for many researchers and funders, amfAR has funded cure research for more than 10 years and has supported some of the most important such work to date, including the characterization of the Berlin patient,¹⁰ the Mississippi child,¹¹ and the Boston patients,¹² as well as basic research findings describing the lack of viral evolution in reservoirs,¹³ a comparison of assays to measure the size of the viral reservoir,¹⁴ the lack of killing after viral reactivation,¹⁵ and the characterization of noninduced proviruses.¹⁶ There has been growing optimism within the scientific community that with the necessary resources, a cure—long thought impossible—might be achievable within our lifetime. Unfortunately, U.S. budget sequestration and a steady decline in the purchasing power of the National Institutes of Health over the past decade have had adverse effects on the number and the budgets of the grants funded.

AIDS Research and Human Retroviruses continues to track progress being made in the search for an AIDS vaccine.^{17–19} Yet there are other means of decreasing HIV transmission.²⁰ Condoms, when used consistently and correctly, decrease the likelihood of transmission by 85% or more.²¹ Syringe exchange programs reduce the sharing of needles and have brought HIV transmission among injection drug users almost to zero in New York City.²² Even antiretroviral therapy, used either as preexposure prophylaxis,²³ as a topical application,²⁴ or for the early treatment of the infected partner in serodiscordant couples,²⁵ drastically reduces the spread of the virus. However, ideological squeamishness (in the case of condoms and syringe exchange) and lack of political will threaten our ability to put those hard-won scientific insights to work.

Improving public health through science requires three basic elements: the generation of new scientific knowledge, the sharing of that knowledge with peers, and the implementation of those interventions that have been proven effective. amfAR and *AIDS Research and Human Retroviruses* continue to play vital roles in the first two. We hope that we can depend on our lawmakers, and on other governments and funders, to deliver on the third.

We look forward to the day when *AIDS Research and Human Retroviruses* will be able to publish the best kind of AIDS story—the one that describes how the efforts of

thousands of researchers working around the world have brought us a world free of AIDS.

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References

- De Clercq E: HIV inhibitors targeted at the reverse transcriptase. *AIDS Res Hum Retroviruses* 1992;8(2):119–134.
- Debouck C: The HIV protease as a therapeutic target for AIDS. *AIDS Res Hum Retroviruses* 1992;8(2):153–164.
- Wild C, Greenwell T, and Matthew T: A synthetic peptide from HIV-1 gp41 is a potent inhibitor of virus-mediated cell-cell fusion. *AIDS Res Hum Retroviruses* 1993;9(11):1051–1053.
- Young B, Squires KE, Ross LL, Santiago L, Sloan LM, Zhao HH, Wine BC, Pakes GE, Margolis DA, Shaefer MS, and the Aries EPZ108859 Study Team: Inflammatory biomarker changes and their correlation with Framingham cardiovascular risk and lipid changes in antiretroviral-naïve HIV-infected patients treated for 144 weeks with abacavir/lamivudine/atazanavir with or without ritonavir in ARIES. *AIDS Res Hum Retroviruses* 2013;29(2):350–358.
- Jansen K, Sönnernborg A, Brockmeyer N, Thalme A, Svedhem V, Dupke S, Eychenne JL, Nakonz T, Jimenez-Exposito MJ, and Pugliese P: Long-term efficacy and safety of atazanavir/ritonavir treatment in a real-life cohort of treatment-experienced patients with HIV type 1 infection. *AIDS Res Hum Retroviruses* 2013;29(3):564–573.
- Albini L, Calabresi A, Gotti D, Ferraresi A, Festa A, Donato F, Magoni M, Castelli F, and Quiros-Roldan E: Burden of non-AIDS-defining and non-virus-related cancers among HIV-infected patients in the combined antiretroviral therapy era. *AIDS Res Hum Retroviruses* 2013;29(8):1097–1104.
- Hsieh SM, Pan SC, Chang SY, Hung CC, Sheng WH, Chen MY, and Chang SC: Differential impact of resistance-associated mutations to protease inhibitors and nonnucleoside reverse transcriptase inhibitors on HIV-1 replication capacity. *AIDS Res Hum Retroviruses* 2013;29(8):1117–1122.
- Reynes J, Trinh R, Pulido F, Soto-Malave R, Gathe J, Qaqish R, Tian M, Fredrick L, Podsadecki T, Norton M, and Nilus A: Lopinavir/ritonavir combined with raltegravir or tenofovir/emtricitabine in antiretroviral-naïve subjects: 96-week results of the PROGRESS study. *AIDS Res Hum Retroviruses* 2013;29(2):256–265.
- Hütter G, Nowak D, Mossner M, Ganepola S, Müssig A, Allers K, Schneider T, Hofmann J, Kücherer C, Blau O, Blau IW, Hofmann WK, and Thiel E: Long-term control of HIV by CCR5 delta32/delta32 stem-cell transplantation. *N Engl J Med* 2009;360(7):692–698.
- Yukl SA, Boritz E, Busch M, Bentsen C, Chun TW, Douek D, Eisele E, Haase A, Ho YC, Hütter G, Justement JS, Keating S, Lee TH, Li P, Murray D, Palmer S, Pilcher C, Pillai S, Price RW, Rothenberger M, Schacker T, Siliciano J, Siliciano R, Sinclair E, Strain M, Wong J, Richman D, and Deeks SG: Challenges in detecting HIV persistence during potentially curative interventions: A study of the Berlin patient. *PLoS Pathog* 2013;9(5):e1003347.
- Persaud D, Gay H, Ziemniak C, Chen YH, Piatak M Jr, Chun TW, Strain M, Richman D, and Luzuriaga K: Absence of detectable HIV-1 viremia after treatment cessation in an infant. *N Engl J Med* 2013;369(19):1828–1835.
- Henrich T, Hanhauser E, Sirignano M, Davis B, Lee T-H, Keating S, Busch M, Marty F, LaCasce A, Armand P, Soiffer R, Altfeld M, and Kuritzkes D: In depth investigation of peripheral and gut HIV-1 reservoirs, HIV-specific cellular immunity, and host microchimerism following allogeneic hematopoietic stem cell transplantation. International AIDS Society conference, 2013, WELBA05.
- Josefsson L, von Stockenström S, Faria NR, Sinclair E, Bacchetti P, Killian M, Epling L, Tan A, Ho T, Lemey P, Shao W, Hunt PW, Somsouk M, Wylie W, Douek DC, Loeb L, Custer J, Hoh R, Poole L, Deeks SG, Hecht F, and Palmer S: The HIV-1 reservoir in eight patients on long-term suppressive antiretroviral therapy is stable with few genetic changes over time. *PNAS* 2013;110(51):E4987–E4996.
- Eriksson S, Graf EH, Dahl V, Strain MC, Yukl SA, Lysenko ES, Bosch RJ, Lai J, Chioma S, Emad F, Abdel-Mohsen M, Hoh R, Hecht F, Hunt P, Somsouk M, Wong J, Johnston R, Siliciano RF, Richman DD, O'Doherty U, Palmer S, Deeks SG, and Siliciano JD: Comparative analysis of measures of viral reservoirs in HIV-1 eradication studies. *PLoS Pathog* 2013;9(2):e1003174.
- Shan L, Deng K, Shroff NS, Durand CM, Rabi SA, Yang HC, Zhang H, Margolick JB, Blankson JN, and Siliciano RF: Stimulation of HIV-1-specific cytolytic T lymphocytes facilitates elimination of latent viral reservoir after virus reactivation. *Immunity* 2012;36(3):491–501.
- Ho YC, Shan L, Hosmane NN, Wang J, Laskey SB, Rosenbloom DI, Lai J, Blankson JN, Siliciano JD, and Siliciano RF: Replication-competent noninduced proviruses in the latent reservoir increase barrier to HIV-1 cure. *Cell* 2013;155(3):540–551.
- [No authors listed]: AIDS vaccine 2013 October 7–10, 2013 Barcelona, Spain. *AIDS Res Hum Retroviruses* 2013;29(11):A1–A208.
- Karasavvas N, Billings E, Rao M, Williams C, Zolla-Pazner S, Bailer RT, Koup RA, Madnote S, Arworn D, Shen X, Tomaras GD, Currier JR, Jiang M, Margaret C, Andrews C, Gottardo R, Gilbert P, Cardozo TJ, Rerks-Ngarm S, Nitayaphan S, Pitisuttithum P, Kaewkungwal J, Paris R, Greene K, Gao H, Gurunathan S, Tartaglia J, Sinangil F, Korber BT, Montefiori DC, Mascola JR, Robb ML, Haynes BF, Ngauy V, Michael NL, Kim JH, de Souza MS, and the MOPH TAVEG Collaboration. The Thai Phase III HIV Type 1 Vaccine trial (RV144) regimen induces antibodies that target conserved regions within the V2 loop of gp120. *AIDS Res Hum Retroviruses* 2012;28(11):1444–1457.
- Klasse PJ, Sanders RW, Cerutti A, and Moore JP: How can HIV-type-1-Env immunogenicity be improved to facilitate antibody-based vaccine development? *AIDS Res Hum Retroviruses* 2012;28(1):1–15.
- Kiser PF, Mesquita PM, and Herold BC: A perspective on progress and gaps in HIV prevention science. *AIDS Res Hum Retroviruses* 2012;28(11):1373–1378.
- National Institute of Allergy and Infectious Diseases, Workshop Summary: Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease (STD) Prevention, July 20, 2001.
- Cohen J: Miracle on 34th Street: Success with injectors. *Science* 2012;337(6091):178–180.
- Baeten JM, Haberer JE, Liu AY, and Sista N: Preexposure prophylaxis for HIV prevention: Where have we been and

- where are we going? *J Acquir Immune Defic Syndr* 2013; 63(Suppl 2):S122–129.
24. Abdool Karim Q, Abdool Karim SS, Frohlich JA, *et al.*: Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science* 2010;329:1168–1174.
 25. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseini-pour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Mehendale S, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-Manning E, Wang L, Makhema J, Mills LA, de Bruyn G, Sanne I, Eron J, Gallant J, Havlir D, Swindells S, Ribaudo H, Elharrar V, Burns D, Taha TE,

Nielsen-Saines K, Celentano D, Essex M, Fleming TR, and the HPTN 052 Study Team: Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365(6):493–505.

Address correspondence to:
Rowena Johnston
The Foundation for AIDS Research
120 Wall Street, 13th Floor
New York, New York 10005
E-mail: rowena.johnston@amfar.org