Editorial & Letters

EDITORIAL

Science and the Control of AIDS

This has been a year worth celebrating for AIDS research. For the first time in the history of the HIV epidemic, after nearly two decades of increasing mortality, the U.S. death rate attributable to AIDS has dramatically declined. Satisfyingly, the explanation is almost entirely based on science: A logical sequence of discoveries and tests has led to highly effective antiviral therapies.

It is commonplace, when citing this triumph, to qualify it by pointing to the many drug failures, the expense of the regimens, the continued high rate of virus transmission in the United States (especially among minority groups), the growing magnitude of the epidemic in the poorer parts of the world (where the successful drugs are simply unaffordable), and the difficulties of developing an effective HIV vaccine. But before addressing these serious problems, it is valuable to contemplate the success itself, because it illustrates principles that extend well beyond HIV.

The progress made against HIV exemplifies the potency of molecular medicine—based, in this case, on full disclosure of viral genes, analysis of viral dynamics and pathogenesis, and development of protein-targeted drugs. This is strong evidence that the prospects are bright for rational treatments of many other complex disorders once we understand their genetic origins and pathophysiological mechanisms. Ongoing efforts to decipher the genomes of humans and microbes and to understand how cells cycle, signal, and die are bringing us to a new level of understanding of human biology and disease. If the recent success with AIDS is any guide, this new knowledge will soon transform the practice of medicine.

The challenge of developing treatments for AIDS has also provided a test of our biomedical research establishment, in which federal agencies and private foundations largely fund investigator-driven basic science, the pharmaceutical industry and biotechnology companies undertake most drug discovery and development, and these two components interact to transfer knowledge and foster its application. The recent success has affirmed the vigor of this system. Basic research, some dating back well before the advent of AIDS, recognized retroviral enzymes that are essential for replication and pathogenesis; medicinal chemistry, informed by structural biology, generated many enzyme inhibitors, a few of which survived rigorous screening to become the drugs now prolonging the lives of AIDS patients. This experience can serve as a paradigm for controlling other chronic progressive diseases.

We must also acknowledge the limits of the therapeutic success and speak to the challenges that remain. First, there is a need for improved versions of current drugs—for drugs that are longer acting or better tolerated in order to promote adherence to complex regimens, and drugs that are less expensive and more practical for use in developing countries. A better understanding of viral variation might also help us cope with drug resistance. Active research programs are needed to seek classes of compounds targeted against other viral functions, with the prospect of complementing existing drugs. In addition, behavioral research has the potential to improve compliance with current regimens, as well as to enhance current strategies to reduce transmission.

A safe and effective vaccine is probably the single most important long-term goal of current research efforts. A vaccine that fully prevents the establishment of HIV infection, however, is a daunting and perhaps an impossible goal; even one that offers significant reduction of disease and mortality appears to be a difficult task, judging from the limited progress thus far. The National Institutes of Health (NIH) has committed increasing resources to the challenge of developing an AIDS vaccine, while working in concert with other federal and private agencies and with industry, in the United States and abroad. We have expanded a program that enhances current understanding of the immune response to viral antigens; seeks candidate immunogens; tests them in primate (and perhaps other animal) models; and then evaluates safety, delivery, and efficacy in clinical trials of the most promising candidates. We recognize the magnitude of this challenge and the fact that it may well be necessary to deploy vaccines that have modest efficacy while simultaneously developing future generations of more effective immunogens. But we also believe that the still-expanding global dimensions of AIDS are likely to be checked only if science can succeed as admirably with vaccines as it has done with therapies.

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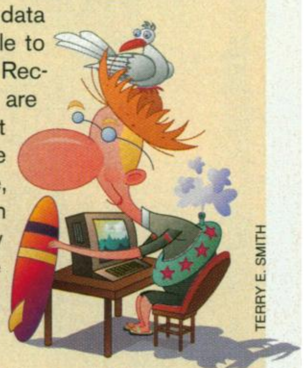
LETTERS

The endless search



Are scientific data easily accessible to Web surfers? Recommendations are put forth about what should be posted, where, and how it can be permanently archived. The practicality of tokamak fusion is questioned. The function of the cerebellum is explored. And observations about progression from HIV infection to AIDS are clarified.

Access to Information on the Web

Y. Poumay's letter of 22 May, (p. 1173) raises an important and often discussed question about the persistence of scientific and technical information on the World Wide Web. What is often forgotten is that one of the early motivations for developing the Web was to provide easy access to scientific data for more scientists. This trend is continuing in many areas where recent results are published and posted for all to read and use (for example, the Los Alamos National Laboratory e-Print Archive, http://xxx.lanl.gov/). It could even be argued that information on the Web is far more accessible than that in libraries for most scientists.

We believe that references to possibly short-lived material should be avoided when possible, but such references are better than omitting relevant work. References to the Web in addition to traditional references can also make material more readily obtainable by scientists. More important is the issue of ensuring that scientific material is long-lived and easily accessible, regardless of whether it exists online or in traditional media; for example, see the Persistent Uniform Resource Locator service (http://purl. oclc.org/) or the Handle System (http:// www.handle.net/). Also, the archival intermemory project (*1*) at the NEC Research Institute hopes to provide an Internet-distributed memory resource that would enable robust archival information storage on the Web.

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