

AIDS — a treatable disease at last

Progress in the clinical treatment of AIDS parallels the stories of failure followed by success that marked the first decade in the "War on Cancer." This issue of *Nature Medicine* is a paean to perceived success in the treatment of AIDS: advances that have occurred within the past few years, and even the past few weeks. It is a remarkable and, one hopes, true story.

The first good news about AIDS in 1984 was when the human immunodeficiency virus was pinned down as the etiologic agent and an accurate test to identify HIV in blood was approved for market. The optimism that followed, based on the reasonable and fervent hope that an AIDS vaccine would be forthcoming, proved unjustified. Similarly, early hopes that AZT would cure the disease or significantly prolong productive life did not materialize. And so, the AIDS story has been one of medical disappointment, coupled with high political drama, as dying AIDS patients and their friends and families blamed allegedly stingy governments and indifferent scientists for the lack of a cure.

Virtually everyone felt down. But suddenly the mood has changed. At a meeting on retroviruses that was held in Washington just a few weeks ago (pp. 257 and 274), a consensus emerged on data that have been accumulating for a couple of years — beginning with a 1995 paper in *Nature* suggesting that the critical indicator in HIV should be the quantity of virus a patient carries (the so-called viral load) rather than the concentration of CD4 immune cells in serum. Now there is fair agreement that it is critical in AIDS to reduce the viral load, just as it is important to wipe out bacteria or fungi in other diseases.

Equally important, therapy with new protease inhibitors provides an effective way to do just that. A combination drug regimen including protease inhibitors and existing anti-AIDS drugs seems to offer a medical approach that makes a significant difference in the length and quality of patients' lives. An equally important observation is that patients who are cared for by physicians who are experienced in the nuances of AIDS therapy do better clinically than those whose doctors are in general practice.

Another interesting, if perplexing, part of the present excitement about AIDS is the story of Jeff Getty, the activist who recently received a transplant of bone marrow from a baboon in the hope that new marrow from an HIV-resistant baboon would reconstitute his failing immune system (p. 259). Although there is no evidence from the baboon cells engrafted in Getty's

marrow, the patient is doing better, prompting new ideas for future experimentation.

In terms of both drugs and transplantation, the analogy to what in the United States is the so-called multi-billion dollar "War on Cancer," is inescapable. More than 30 years ago, frustration with progress in the treatment of malignancy led to a highly politicized and publicized attempt to cure cancer once and for all by declaring war on a biological phenomenon as if it were a military enemy.

It is easy to forget that chemotherapy as a successful modality for malignancy is really quite new, and that the progression from the use of one agent to several in carefully calibrated combinations set the pattern for drug therapy of AIDS. In the 1960s, only a handful of hospitals were at the forefront in the experimental use of chemotherapeutic agents. Those on the front lines in the treatment of now curable cancers such as childhood leukemias saw many patients die from the toxic effects of methotrexate and other then-novel agents. Furthermore, just as with AIDS, there was a steady progression in drug therapy from the use of single agents to combination treatment, including combinations of surgery and radiation with chemotherapy, before really useful clinical results were achieved.

Neither rhetoric nor money has cured cancer. However, there can be no doubt but that today most cancer patients stand a fighting chance of surviving at least the first round with their disease. Many survive second and even third recurrences, while other cancer patients are genuinely cured.

It would be sheer folly to suggest that what looks like significant clinical progress in AIDS brings us close to any ultimate resolution of the battle against this intrepid disease. Protease inhibitors have still to prove themselves in thousands of patients: the cost of these agents, which run to thousands of dollars a year, will have to be brought down. The cost of high-technology medical care is a serious issue in all of the developed nations. But it is the poorer nations of Africa and Asia that are likely to be decimated as the AIDS epidemic continues.

The plain fact is that the biology of diseases such as cancer and AIDS that follow a relentless course through multiple organ systems is still beyond medicine's understanding. So while we congratulate the researchers who have brought us where we are today, we continue to await with eager anticipation the insights of the next generation.

— Barbara J. Culliton

Finally, clinical progress that really makes a difference.