EDITORIAL

AIDS 1993: Unanswered Questions

No issue focusing on acquired immunodeficiency syndrome (AIDS) should begin without a reminder of the frightening power and magnitude of the disease. The World Health Organization estimates that roughly 13 million people have been infected with human immunodeficiency virus (HIV) and that by the year 2000, that number may triple. A fitting memorial for those who have died would be the knowledge that there was a cure or a vaccine at hand—that no one else would have to endure the inexorable suffering and death. But how close are we?

This issue attempts to clarify the state of the art and indicates some of the areas of uncertainty, both scientific and social, that will need to be faced. Robin A. Weiss in his article likens the investigation of how HIV causes AIDS to the group of blind men trying to identify an elephant by feeling the different parts. Everyone is focusing on a small piece of the puzzle but no one has yet been able to put it all together. In a special news section, Jon Cohen has asked prominent scientists to define the most important questions to be addressed in developing a cure or a vaccine. The range of responses indicates how many fundamental questions are still unanswered.

In vaccine research, a key question is, "What kind of immune response represents a successful battle against the disease?" As reviewed by Barton F. Haynes, candidate immunogens are being developed that will induce some or all of the immune responses that could be efficacious. Different approaches to successful protection can be found in the Reports and Perspectives sections. The testing of candidate vaccines that may not be 100% effective raises social issues that must also be addressed.

Right now the best approach to preventing AIDS lies in behavior modification, a necessary but less-than-perfect strategy. Michael H. Merson discusses the different mechanisms for promoting safer behavior, ranging from repeated educational messages about AIDS to spermicides with antiviral capacity that can help empower women worldwide. The need for more effective education must not be ignored. Currently, condoms can be an effective, prophylactic vaccine. Therefore, in order to protect our teenagers, a major component of our AIDS strategy should be an intelligent program of sex education in the schools.

Although many stages in the viral life cycle are being probed as possible targets for therapeutic agents and many different drug design approaches are being explored (as discussed by Margaret I. Johnston and Daniel F. Hoth), we are still a long way from having something that will stop progression to AIDS. There is still no certainty even that the best surrogate markers have been found to evaluate effectiveness of therapeutic agents or that the peripheral blood is the most physiologically relevant place to look. Viral variation and the rapid development of drug resistance are still enormous hurdles.

This issue contains two perspectives that are sure to provoke debate. Jonas Salk and colleagues present their view that AIDS, like such diseases as leishmaniasis and tuberculosis, can only be controlled by the early "locking-in" of cell-mediated immunity, specifically through T helper 1 (T_H1) cells. They raise the spector that the development of an antibody response signals a loss of protective capability and also present several strategies that could push the immune system toward a T_H1 response. Marie-Lise Gougeon and Luc Montagnier discuss their view that apoptosis is the cause of CD4 depletion and the therapeutic consequences of that model.

The rate of scientific progress in identifying HIV and understanding its life cycle and molecular biology are unprecedented in the history of biology. Significant advances have been made in fighting the opportunistic infections associated with AIDS, such as *Pneumocystis carinii*. However, we are not yet at the refinement stage in our fight against the virus; optimization of a treatment protocol with a proven antiviral agent or vaccine is a distant goal.

The importance of basic research in answering the fundamental questions that remain cannot be minimized. A cure may very well come from an approach that has not been considered yet. Finding such an approach will require open-mindedness, a willingness to challenge accepted dogma, and a high degree of trust and collaboration among researchers from many disciplines, HIV-infected individuals, government, and industry.

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