HIV Pathogenesis and Implication for Therapy

David D. Ho, M.D.

It is safe to say that the global aids epidemic will get much worse before it gets any better. Sadly, this modern plague will be with us for several generations to come, despite the major scientific advances of the recent past and near future.

At the beginning of the new millennium, the AIDS epidemic had already claimed 22 million lives, while leaving 40 million persons living with a viral infection that slowly but relentlessly erodes the immune system. Accounting for over 3 million deaths in the year 2000 alone, the AIDS virus has become the most deadly microbe in the world, exceeding even TB and malaria. There are now 34 developing countries wherein the prevalence of this infection is 2% or greater. In Africa, nearly a dozen countries have an infection rate higher than 10%, including 4 southern nations where a quarter of their citizens are already infected. And the situation continues to worsen, with over 5 million new infections worldwide in 2000. This number is figuratively akin to sentencing 16,000 people each day to a slow and miserable death.

Fortunately, the AIDS story has not been all gloom and doom. Within two years of recognizing AIDS as a new syndrome in 1981, the causative agent - now called human immunodeficiceny virus or HIV - was identified. Shortly thereafter a blood test became widely available in developed countries, along with the first effective drug, AZT. The scientific community now knows more about HIV than any other virus, and 15 AIDS drugs have been developed and licensed in the United States and Western Europe. The effective use of some of these drugs in combination has resulted in unprecedented control of HIV replication in many infected patients, resulting in restoration of the immune system and dramatic declines in AIDS deaths in the better developed countries.

But as we look ahead, AIDS will become even more devastating ъ sub-Saharan Africa, particularly in the south. It will be by far the major killer of young Africans; decreasing life expectancy to as low as 40 years in some countries and single handedly erasing the public health gains of the past 5 decades. In addition to the massive human toll, the epidemic will threaten the socioeconomic and political fabric of numerous nations on the continent. The growth of the epidemic in South America and Eastern Europe will remain severe. The global picture of aids, however, will be influenced most by developments in Asia because of its huge population at risk. The magnitude of the pandemic will be influenced greatly by what happens in India and china. India already has 3-4 million infected persons, but the prevalence of infection is likely to reach a few percent in a population of 1 billion. Over 850,000 Chinese are now infected, but the trajectory of its epidemic is the coming decades, although worrisome, is less certain.

An explosive AIDS epidemic in the United States is unlikely. Instead, HIV infection will continue to fester at a level of about 0.5% of the pollution, but the complexion of the epidemic will change greatly though. New HIV infection will occur predominantly in the underclass, with rates being 10 times higher in minority groups. Nevertheless, American patients will live quality lives for decades, thanks to advances made in medical research, dozens of powerful and well-tolerated AIDS drugs will be developed, as will novel means to aid the restoration of the immune system. A cure for AIDS in the long run is not inconceivable. Bu constrained by economic reality, these therapeutic advances will only have limited benefit in regions beyond the U.S. and Western Europe.

The development of a vaccine to block the continued spread of HIV is our only real hope to avert a global disaster unparalleled in medical history. A concerted effort in vaccine research in the U.S. was launched several years ago under a presidential directive. Hints of promising vaccine strategies are already emerging from recent experiments in monkeys. There is renewed confidence that the talent and creativity of biomedical scientists will produce a productive aids vaccine in the coming years. But the eventual elimination of aids will also require the political will o four world leaders to acknowledge the enormity of this human crisis and to make the necessary commitment of research.

David D. Ho, M.D. is director and CEO, Aaron Diamond AIDS Research Center and Irene Diamond Professor, The Rockefeller University.