



## HIV and the Pathogenesis of AIDS

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Several times in his disturbing book-made-TV-movie *And The Band Played On*, the late Randy Shilts describes the bureaucratic funding barricades that prevented Jay Levy at the University of California at San Francisco from pursuing research on the causal agent of AIDS. Despite the numerous hurdles decried by Shilts, Levy and his collaborators managed to overcome enough of them to be one of the first groups to isolate human immunodeficiency virus (HIV), naming it AIDS-associated retrovirus (ARV). Now Levy has written a book of his own, *HIV and the Pathogenesis of AIDS*, an attempt to synthesize everything known and theorized to date about how HIV causes AIDS.

Perhaps more than anything else, Levy's new book makes it clear that funding is no longer the real problem in understanding AIDS pathogenesis. When one despairs of the apparent slow pace of research — at least when measured against the continued rounds of loss of friends and acquaintances to the disease — leafing through this book is therapeutic. The number of re-

searchers, the amount of work they've done, and how much they've learned overwhelms. Levy chronicles in numbing detail the inconceivable complexity of the virus and its multiple interactions with its hapless host at all levels of pathogenesis. He begins with a description of the virus itself, then traces its deadly effects from the initial steps in infection through viral replication and host immune responses, ending with implications for antiviral therapy design. Levy backs up his recital with 2,000 references culled from the nearly 100,000 reports and articles published since HIV was first described.

Levy's thoroughness — and writing style — conversely reveals just how far researchers have to go. For example, in a chapter entitled "Early Steps Involved in HIV Infection," Levy describes studies performed with soluble CD4 (the T cell receptor used by HIV to enter the cell) and their relevance to *in vivo* neutralization:

In perhaps related observations, some freshly isolated HIV-1 strains, usually macrophage-tropic, have shown reduced susceptibility to sCD4 inactivation. The reason for this resistance, reflected in some isolates by up to 1000-fold higher concentrations of sCD4 needed for inactivation, is not well defined. As noted above, the findings could reflect less efficient binding of virus to sCD4 and/or lack of gp120 shedding (or displacement) following the interactions with sCD4. Similar suggestions have been made to explain the relative effectiveness of antibody neutralization and enhancement.

These careful, qualified statements are the language of science, and they demonstrate how tentative scientists must be in drawing conclusions. But they are also difficult to read for sustained periods. The ever-present qualifications and considered caveats tend to water down important observations while appearing to overstate the importance of others. Unfortunately, this leaves the reader to weigh the relative worth of different observations. This is something that should be addressed in any future editions of the book.

Providing a better historical perspective, something Levy hints at in the introduction, would also be an improvement. More than a chronological listing of discoveries, "history" includes the human side of the scientific undertaking. In Levy's book researchers are often reduced to numbered references, and those that

are mentioned by name are usually described as impartial observers of diverse phenomena. Most AIDS researchers will say (off the record) that the field is particularly competitive and even nasty at times, but that contributes to its excitement. Granted, this probably is not what Levy set out to write, yet researchers are hardly the dispassionate observers he describes.

Along the same lines is the nearly complete lack of reference, except in the most clinical terms, to the terrible toll of human suffering exacted by AIDS. As one of the first physicians to work with AIDS patients, Levy is hardly unaware of the terrors of the disease. This is what should give AIDS research urgency, not simply the quest to understand pathogenesis or to receive the notoriety that comes with discovery. In a book that will doubtless become a primary reference for many new as well as current researchers, this could be a helpful reminder.

As a work in progress, the book inevitably has gaps, some notable. They highlight the difficulty of writing about a field that is constantly changing. Recent work disclosing the frantic daily turnover of virus and CD4-positive T cells in infected people is missing. New publications from several research groups describing host factors in long-term non-progressors are also unreferenced. Undoubtedly these will be incorporated in any future editions of the book.

*HIV and the Pathogenesis of AIDS* is not a 'page-turner.' But as a reference work, it is valuable. Anyone familiar with the field and in need of relatively up-to-date (as of August 1994) information about what scientists know about how HIV causes AIDS will find this book worth reading. Those recalcitrant people who continue to believe that AIDS is the result of some agent other than HIV would also do well to read it and learn how definitive are the ties between the virus and the disease. And those who preach that HIV was manufactured by scientists for genocidal reasons will, by thumbing through just the chapter on the heterogeneity of HIV, be struck by the exquisite complexity of the virus and realize just how far-fetched are their beliefs.

*HIV and the Pathogenesis of AIDS* is ultimately a snapshot of the moving target of AIDS research. In the introduction Levy writes that he hopes his book "will provide the foundation for future work that will find the solution to this devastating problem." Though the book itself may not, the research it chronicles undoubtedly will, and, we hope, soon.