AIDS meeting suggests basic research gaps

The more than 3,100 scientific presentations at the Fourth International Conference on AIDS meeting in Stockholm last week had a most curious effect. Individually, each spoke of a small advance in the science of the human immunodeficiency virus (HIV), which causes the disease. But taken together, they suggested some potentially serious flaws in the direction of AIDS research.

Nowhere was this more apparent than in vaccine development. Over the past five years, scientists have expended tremendous effort to decipher HIV's entire genetic code. One major goal is to use this information, together with genetic engineering, to develop a vaccine. Half a dozen genetically engineered AIDS vaccines already have emerged from laboratories, and two have triggered some immune response in human beings. But it's far too early to say whether that response in any way provides a defense against the living AIDS virus.

Daniel Zagury from the University of Paris in France, the first person to inject himself with an AIDS vaccine, reported in Stockholm that he plans to expand his test later this year. He expects to inject the vaccine into hundreds or thousands of people in Africa — exactly where or what group of people, he refuses to say.

He also says he plans to give his vaccine to pregnant women infected with HIV to see whether they will pass immunity along to their unborn children. The second vaccine tested in human beings, developed by the National Institutes of Health and MicroGeneSys in West Haven, Conn., has fairly minor side effects, reported H. Clifford Lane from the National Institute of Allergy and Infectious Diseases (NIAID).

But it will take studies with hundreds, perhaps thousands of volunteers followed over many years to determine whether these vaccines are effective. So it's crucial for AIDS vaccines to be based on the soundest theories. One index of a theory's strength is success in animal studies. Yet, experimental genetically engineered AIDS vaccines have failed to protect lab animals from infection. As a result, some scientists are having second thoughts about this high-tech strategy to AIDS-vaccine research. Indeed, although HIV was isolated five years ago, only now are scientists conducting the classic vaccine experiments: killing the virus, then injecting it into chimpanzees to see if the killed virus acts as a vaccine.

"I think we've done what we call in the United States 'home-run-strategy' research so far," says Jorg Eichberg, a vaccine researcher from the Southwest Foundation for Biomedical Research in San Antonio, Tex. "Now [with these chimpanzee studies], I think we're going back to the basic research where we try to put the mosaics together one by one."

AIDS has attracted disproportionate attention from molecular biologists, who study the virus from the standpoint of its genetic instructions, says David Baltimore from the Whitehead Institute for Biomedical Research in Cambridge, Mass. Comparatively less effort has gone into the basic virology: studying the AIDS virus as a virus.

The molecular approach to vaccines was seductive because if a genetically engineered vaccine works, it is most likely safe. Most scientists have avoided the killed AIDS virus because viruses might survive and cause disease instead of preventing it.

Donald Francis, a U.S. Centers for Disease Control researcher working at the California Department of Health Services in Berkeley, says that is a poor reason to have skipped the chimpanzee studies. If the killed-virus vaccine protects the chimps from infection, Francis argues, researchers could possibly use that information to design a safe, genetically engineered vaccine.

But Jonas Salk, who developed the first polio vaccine, contends the safety issue has been overblown. He has killed the AIDS virus with radiation and freeze-dried it. The resulting vaccine has been injected into volunteers at the University of Southern California (USC). People in this experiment already are infected with HIV, so safety is not an overriding issue. Salk hopes the vaccine will work as a therapy in these people, by boosting their natural immune response to the AIDS virus and keeping the disease from spreading in their bodies.

Alexandra Levine at USC reported the vaccine caused no ill-effects in nine men who were followed for up to seven months. So she and Salk have begun giving the vaccine to 54 more HIV-infected people to see whether it prevents the disease's progression.

Drug development is another area of glaring gaps in the fundamental science of AIDS. Researchers in Stockholm were particularly abuzz about a drug called soluble CD4. This drug is based entirely upon a theoretical understanding of how the AIDS virus makes its way into cells. Scientists have amassed considerable evidence to show the AIDS virus only infects cells that display a molecule on their surface called CD4. In theory, if enough soluble CD4 is present, wandering AIDS viruses are more likely to bind to the drug than to infect another cell. And that should take the virus out of circulation.

Test-tube experiments are encouraging. Several labs reported that soluble CD4 prevents the AIDS virus from infecting cells of the immune system. And Jerome Groopman's laboratory at the New England Deaconess Hospital in Boston reported CD4 does not interfere with the normal workings of the immune system, as some scientists had feared.

Robin Weiss from the Institute of Cancer Research in London, however, reported a potentially serious flaw in the CD4 strategy. His studies suggest HIV doesn't always rely on CD4 to get into cells. Despite treatment with soluble CD4, the AIDS virus was still able to invade a type of brain cell called an astroglial cell. So soluble CD4 may not be able to prevent AIDS-related dementias.

Other researchers presented very preliminary findings suggesting the importance of CD4 has been overstated. Malcolm Martin and his colleagues at NIAID have genetically engineered a mouse that has, in effect, the AIDS virus lodged in every single cell of its body. The mouse doesn't have any CD4 molecules at all, yet the virus still appears to be active in the immune system, Martin announced.

Exactly what this means is unclear, but at the very least it appears CD4 molecules only partly explain why the AIDS virus ravages immune-system cells. Martin plans further experiments on his engineered mouse strain, which is the first lab animal that actually gets sick and dies as a result of the human AIDS virus.

Richard F. Harris, science reporter for National Public Radio, wrote this report from the AIDS meeting in Stockholm.

HIV panel completes report

The Presidential Commission on the Human Immunodeficiency Virus (HIV) Epidemic, in finishing its final report last week, recommended freeing the National Institutes of Health's efforts to oversee AIDS research from the strict supervision of the Office of Management and Budget. The 13-member panel also suggested that manufacturers of an AIDS vaccine and physicians who test it be protected from excessive legal liability.

After reviewing public comments on their draft report, commissioners added a recommendation for a registry to hold findings from clinical trials.

The 300-page document emphasizes that public health officials should devote their attention to the entire spectrum of HIV virus infection, not just to people who have developed the disease.

"Did everybody note that we have just achieved a major milestone?" remarked chairman James Watkins as commissioners approved the 11th chapter of the 300-page report due on President Reagan's desk June 24. Deleted from the final report were Watkins' stern criticisms of the federal government's handling of the epidemic (SN: 6/11/88, p.372). □