Salk maps plan for an AIDS vaccine

by John Grauerholz, M.D.

Dr. Jonas Salk, developer of the first effective polio vaccine, has proposed the first comprehensive strategy to prevent the development of AIDS in already-infected individuals. In an article in the June 11, 1987 issue of *Nature* magazine, Salk argues that preventing the development of AIDS in already-infected individuals would have a greater impact on disease and death from HIV (Human Immunodeficiency Virus) than immunizing uninfected individuals. In addition, if immunization of seropositive virus carriers reduced their contagiousness, this would rapidly decrease the virus reservoir in the population and slow the spread of the disease.

This is a radical departure from the current line of the World Health Organization and other malthusian organizations, which write off the 100 million persons who will probably become infected over the next five years.

One approach to the problem would be to compare the immunological profiles of healthy infected persons, with those of AIDS and AIDS Related Complex (ARC) patients. Understanding why disease does not develop in some healthy carriers, would provide leads to immunologic interventions that could prolong the disease-free state.

One clue to the resistance of some infected individuals to development of disease, relates to certain antibodies which are formed in all infected individuals, but are subsequently lost in individuals who become ill. Virus-neutralizing antibodies, which normally should protect against infection, are present in healthy carriers and also in AIDS and ARC patients. On the other hand, antibodies to p24, a protein which forms the inner protein capsule of the virus, decline as the person becomes ill. Another antibody, to the reverse transcriptase enzyme of the virus, also declines with the onset of illness.

The anti-p24 antibody correlates with a phenomenon known as antibody dependent cell cytotoxicity (ADCC), in which cells known as macrophages recognize and destroy virus-infected T-4 cells. In the early stages of infection, this would prevent the spread of virus and virus proteins, but later on this same process would destroy infected T-cells as well as cells with virus proteins on their surfaces. This would lead to depletion of the T-4 cells at a more rapid rate than they can be replaced, as well as self-destruction of antibody-dependent cell cytotoxicity associated with loss of the anti-p24 antibody.

If the persistence of antibodies to p24 and reverse transcriptase prevents the development of AIDS, then, Salk believes, it may be possible to boost the level of these antibodies by an appropriate immunization. This is known as an anamnestic response, in which the body "remembers" a previous exposure to an immunizing antigen, or immunogen. This anamnestic response is the basis of "booster" shots, which amplify and sustain the antibodies produced in response to an initial immunization.

Salk proposes to enhance protective factors produced by the initial immune response to infection, by administering a potent, noninfectious, immunogen to seropositive virus carriers. Such an immunogen would be prepared from killed whole virus (like the Salk polio vaccine), or a mixture of virus antigens produced by genetic engineering, combined with a chemical known as an adjuvant—a substance, such as mineral oil, which markedly enhances the immune response to an antigen.

Because of its long latent period, the AIDS virus is potentially susceptible to a vaccine administered after infection has occurred. Similar vaccines have been developed already for rabies and hepatitis-B, diseases in which the body can respond to vaccination before the infecting agent has a chance to produce disease.

Science bureaucracy is skeptical

The reaction of the scientific establishment to Dr. Salk's proposal, reported in the *New York Times* of June 11, was less than enthusiastic. According to Lawrence K. Altman, the *Times'* AIDS specialist: "Scientists warned that it could take months or years to lay the scientific groundwork for the approach proposed by Dr. Salk, and longer to prove its safety and effectiveness. Extensive research on animals and humans to identify the key protective factors is required. A major problem in testing any AIDS vaccine is that only one animal, the chimpanzee, can be infected with the AIDS virus, and chimpanzees do not develop the fatal disease."

The fact that chimpanzees infected with the AIDS virus do not develop AIDS is beside the point. As Salk observes, "Animal models presently exist in chimpanzees—infected with HIV—to test for the effects of an immunogen administered post-exposure, in terms of anamnestic response and virus carriage, and to be certain that unexpected adverse effects do not occur in such animals. But the ability of immunization to prevent disease can only be answered by studies in human subjects who are already infected. Toward this end, appropriately designed immunogens are required to be tested in serologically positive (HIV) healthy individuals who are at risk of developing AIDS and who are also a source of contagion to others."

If this sounds a little different than the usual blather on the subject, perhaps it is because Salk is a scientist who has actually conquered an epidemic disease, and not a bureaucrat placating special interest groups.