

Medicine by John Grauerholz, M.D.

AIDS: Jenner to the Rescue?

The Vaccinia research shows there is no shortage of ingenious approaches to disease, if the political will exists.

Two recent articles in *Nature* magazine (April 10, 1986) describe expression of the envelope gene of the AIDS virus, HTLV-III/LAV, in a recombinant Vaccinia virus. Vaccinia, a pox virus which used to cause a mild disease of milkmaids called cowpox, was the agent used by the father of immunotherapy, William Jenner, to inoculate people against smallpox. The term vaccination comes from the name Vaccinia given to this virus.

Smallpox vaccination has been discontinued on orders from the communicable diseases division of the World Health Organization, except in the U.S.S.R., which occupies all the senior positions in that division. Nonetheless, researchers at the laboratories of the New York State Department of Health reported some years ago that the Vaccinia virus was capable of being genetically engineered to express multiple viral antigens. The implications of this for vaccine development are enormous.

In principle, the idea of vaccination is to use weakened, or killed, viruses, or parts of viruses, to stimulate the body to make antibodies to a particular virus. The virus or fragment which is used is called an antigen. An antigen is a chemical, usually a protein or a glycoprotein, which stimulates the immune system to make a chemical, called an antibody, which will recognize the antigen and bind to it. If the binding of the antibody to the antigen kills the virus, or inactivates it, the antibody is known as a neutralizing antibody.

Use of live viruses is sometimes associated with eruption of the disease which the vaccine was designed to prevent. This has occurred with the oral polio vaccine, which has been the subject of a number of lawsuits. Use of dead virus tends to eliminate this problem, but ideally one would like to be able to administer only that part of the virus which is needed to stimulate neutralizing antibody production, in sufficient quantity to provoke a good antibody response.

The ability of the Vaccinia virus to express up to eight different viral antigens creates the potential to immunize against multiple viruses with one vaccination, without the risk of getting any of the diseases associated with these viruses, since only the antigens, and not the whole viruses, except for the Vaccinia virus itself, are used. The advantage of a live virus, such as Vaccinia, is production of sufficient antigen to provoke a good antibody response. In this case one gets high production of only the specific genes inserted into the Vaccinia virus. For the AIDS virus, a slow acting virus which directly attacks the immune system, the ability to produce high titers of antibody to the immunogenic envelope protein, without having to use whole virus, is significant.

One way in which the AIDS virus evades the patient's immune system is a very low level of expression outside of cells, so that by the time antibodies are present, virus proliferation is far advanced and the virus is already inside cells, where antibodies are unable

to reach it.

Two groups, one working out of the National Institute of Allergy and Infectious Diseases and the National Cancer Institute, and the other out of the biotech firm Oncogen and the Virology Division of Usamriid in Frederick, Maryland, were able to insert the gene for the outer envelope of the AIDS virus into a Vaccinia virus and then get the gene expressed in infected animals. No other AIDS virus genes were expressed in these animals. Sera from these animals reacted with AIDS virus envelope proteins, and sera from AIDS patients reacted with the Vaccinia product.

While this is a promising avenue toward developing a vaccine which may keep uninfected persons from being infected by the AIDS virus, it will do nothing for those now infected or who will become infected in the meantime. By its very nature, vaccination stimulates the immune system, and evidence is growing that immune stimulation is the trigger that activates AIDS infected cells to produce virus and die. Further, development and testing of such a vaccine would require much larger resources than the present austerity policies of the administration would ever allow. And who knows, maybe the World Health Organization would disapprove?

The point about the Vaccinia research is that there is no shortage of ingenious, and potentially very effective, approaches to AIDS and other diseases, if the political will to confront the problem is present. Jenner was attacked by the spokesman of the drug bankers of his day, the British East India Company's Thomas Malthus, for interfering with God's will by preventing smallpox. The present approach of the Reagan/Regan administration show us that Jenner's adversaries are still with us.