

## Virus-associated immunopathology : animal models and implications for human disease\*

### 1. Effects of viruses on the immune system, immune-complex diseases, and antibody-mediated immunologic injury

*The tissue damage caused by virus infection has been traditionally explained by the ability of viruses to multiply in cells and thereby injure or destroy them. Recent evidence suggests, however, that lesions may also be caused by the host's immune response to viral antigens and that the immune system itself may be perturbed by some viruses. This memorandum reviews recent developments in viral immunopathology, with special reference to animal model systems, and indicates the possible relevance of the new concepts and techniques for certain diseases of man. Certain viruses, notably the leukaemia viruses and some of those causing persistent infections, depress the host's ability to mount an antibody response to antigens, while other viruses may enhance the antibody response. Cell-mediated immunity may also be depressed. Another immunopathological manifestation of virus infection is immune-complex disease. When viruses or their antigens persist in the circulation they combine with specific antibody, and the resulting complexes lodge in various sites, especially the kidney. Further combination with complement leads to the release of tissue-damaging substances. A third condition associated with virus infection is antibody-mediated immunologic injury. Both oncogenic and non-oncogenic viruses frequently induce new antigens on the surface of the cells they invade. When antibody attaches to these antigens in the presence of complement, the cells are destroyed.*

The lesions associated with virus infections have traditionally been explained by the ability of viruses to replicate in cells and hence cause cell injury and even death. However, recent studies indicate that virus-associated tissue damage may be due in part to the immune response of the host to viral antigens. The properties of viruses are seemingly ideal for producing immunopathological damage. Viruses are foreign antigens and, being self-replicating, can continue to produce antigen for long periods of time. Certain viruses are also known to be able to induce new antigens on the surface of cells they infect. The host's immune system can respond to these antigens.

In view of these properties, immunopathological changes may be initiated by a number of different mechanisms in the course of virus infection:

(1) Certain viruses can infect the cells of the immune system and cause direct immunologic

derangements. Many processes and parameters of immune function may be thus affected, including graft rejection, the induction of immunologic tolerance, antibody production, graft-versus-host reactions, lymphocyte transformation, immunoglobulin levels, phagocytosis, and delayed-type skin reactions.

(2) The host's immune response to viral antigens can lead to the formation of virus-antibody complexes capable of reacting with anti-immunoglobulins, rheumatoid factor, and the components of complement.

(3) New antigens produced by viruses on infected cell surfaces can interact with specific antiviral antibody plus complement, thus causing cell destruction.

(4) Recent findings suggest that sensitized lymphocytes can also react with virus-induced cell surface antigens and destroy the cell. Furthermore, cell-mediated (or antibody-mediated) immune responses to viruses may result in the release or activation of biological mediators causing immunopathological changes.

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\* This memorandum was prepared by the signatories listed on page 262.