OVERVIEW OF THE POSSIBLE TARGETS FOR VIRAL CHEMOTHERAPY

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The ideal target for prevention of viral infections is eradication of either the virus or the host, since both are required to produce an infection. For a variety of reasons, mostly personal, we would all agree to preferably eliminate the virus. Such an approach appears to have been accomplished with the world-wide elimination of the virus responsible for smallpox. This was achieved by a highly successful campaign of surveillance and containment by vaccination in order to prevent its spread, rather than by universal routine immunization.

A number of live attenuated vaccines are available not only for prevention of smallpox, which has been eradicated, but more importantly for rubeola (measles), rubella (German measles), mumps, and poliomyelitis. Inactivated vaccines are also available for potential prevention of influenza, poliomyelitis, and rabies (1). In 1981 the U.S. Food and Drug Administration approved a new vaccine for hepatitis B which is produced from hepatitis B surface antigens (HBsAg) found in human blood (2).

Of interest is the development of a vaccine against foot and mouth disease in cattle, swine, sheep and goats caused by a picornavirus. By use of recombinant DNA techniques, the viral RNA coding for VP3, a coat protein, was inserted into an E. coli plasmid, and the desired antigenic protein was produced and purified (3). Two injections of 0.25 mg of this protein produced protection in animals from a challenge dose of virus. However since there are many strains of this virus, about 15 different proteins are expected to be eventually included in order to prepare a comprehensive foot and mouth disease vaccine (3).
An exciting development is the recent chemical synthesis of the first synthetic vaccine to be produced. Peptides were synthesized which corresponded to several regions of the foot-and-mouth disease virus, and one of the peptides (20 amino acids) produced neutralizing antibodies which protected guinea pigs against a challenge with this virus (4). The potential to develop synthetic vaccines for other virus infections is obvious and studies are in progress for development of synthetic vaccines (5–7).

Unfortunately vaccines are not available for all viruses that infect humans and there are a variety of reasons for this. The rhinoviruses consist of over 100 different serotypes and therefore it is most unlikely that vaccination would be a successful procedure for prevention because of the specificity of the immune reaction. A number of compounds however are under consideration for potential therapy of the rhinoviruses and these include arildone, enviroxime, dichloroflavin and interferon.

The influenza A virus presents another problem, in that it continuously changes its antigenic composition, so that this year's vaccine may be less effective against next year's emerging virus. Although amantadine is available for prophylactic or early use against respiratory infections caused by the influenza A viruses, the primary approach is use of the vaccine.

The family of herpesvirus are responsible for a number of clinically important infections:

**HSV-1:** herpes keratitis, herpes encephalitis, mucocutaneous herpes and more recently genital herpes.

**HSV-2:** genital herpes, and possibly cervical cancer.

**Varicella-Zoster:** Varicella (chicken pox) in children, herpes zoster (shingles) in adults and in immunocompromised cancer and organ transplant patients.

**Cytomegalovirus:** Congenital CNS infections. In adolescents and adults an infectious-mononucleosis-like syndrome. In immunocompromised cancer and organ transplant patients it is a major cause of death.

**Epstein-Barr Virus:** Infectious mononucleosis, nasopharyngeal cancer, Burkitt's Lymphoma.

The development of a herpes simplex virus vaccine is under investigation. Inactivated virus cannot be used because of potential oncogenicity. The use of protein-subunits, free of DNA