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Anti-adenovirus Activity of 3'-Fluoro-2',3'-Dideoxythymidine.

JWT Selway, Wellcome Research Laboratories, Beckenham, Kent, UK.

The adenoviruses are a ubiquitous family of viruses of some 41 serotypes which cause upper respiratory infections, eye infections and various enteric disorders. One of the major infections is epidemic keratoconjunctivitis caused by serotype 8. Childhood pneumonias and acute respiratory disease in the elderly institutionalised patient have been known to have fatal sequelae. The onset of AIDS and increasing immuno-suppressive therapies has led to the realisation that adenoviruses may be the agents of more severe disease.

3'-Fluoro-2',3'-dideoxythymidine(3'-FLT) is a potent inhibitor of a number of serotypes of adenovirus. 10 of 12 serotypes thus far investigated are sensitive in the range 0.005-10.0uM. Cell growth inhibition studies indicated in vitro therapeutic indices of 400-12,000. Cell growth inhibition and antiviral activity are reversed by thymidine. Addition of 3'-FLT at variable times during the virus growth cycle correlated with an inhibition of viral DNA synthesis.

3'-FLT is known to be a substrate for cellular phosphorylating enzymes. The triphosphate may inhibit viral polymerase and effect chain termination and thus inhibit replication. This may be consistent with reversal by thymidine. The compound is known to have some toxicity but this may not deter from topical use in epidemic keratoconjunctivitis.