

Effect of Exogenous Interferon on L Cells Persistently Infected with Newcastle Disease Virus

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Prolonged treatment with relatively high concentrations of interferon was required to "cure" L cells persistently infected with Newcastle disease virus.

Thacore and Youngner (2, 3) have described the properties of mouse L cells persistently infected with the Herts strain of Newcastle disease virus (NDV). These cells (L_{NDV}), infected in 1967, continuously produce infective virus (NDV_{pi}), as well as 10 to 30 units of interferon per ml of culture medium; in addition, the L_{NDV} cells are completely resistant to superinfection with vesicular stomatitis virus (VSV). Since NDV_{pi} , the mutant virus present in L_{NDV} cells, can productively infect normal L cells, and since this virus is as sensitive to interferon as VSV when tested in L cells (1), it is paradoxical that NDV_{pi} can maintain the persistent infection in the presence of a concentration of interferon (10 to 30 units) which ordinarily can inhibit its replication.

A study was undertaken to test the effects of exogenous added interferon on the properties of L_{NDV} cells. The interferon used was produced in L cell cultures infected with NDV; the inducing virus was eliminated by treating the fluids at pH 2 at 4 C for 7 days. The details of the methods for preparation of interferon and viruses and for their assay have been documented elsewhere (1, 5).

L_{NDV} cells were subcultured in medium (Eagle's minimal essential medium plus 4% calf serum) to which either 50 or 200 units of interferon per culture was added; control L_{NDV} cells were subcultured in medium without interferon. In the initial phase of this experiment, the monolayer cell cultures were refed daily with interferon or medium. Experience showed this regimen to be unnecessary; therefore, refeeding with interferon or medium was done weekly, at the time the cells were subcultured. The number of cells capable of producing plaques (infective centers) in primary chick embryo cell cultures was determined as described previously (2).

The results in Fig. 1 show that the continuous

presence of 50 units of exogenous interferon in the medium had no significant influence on the frequency of infective centers in the L_{NDV} cell population for the 78-day duration of the experiment. However, with 200 units of interferon in the medium, the number of infective centers gradually decreased until, 35 days after the start of the experiment, no infective centers could be detected in the cell cultures (Fig. 1). These "cured" cell cultures were as susceptible to VSV as normal L cells, and they did not revert to the persistently infected state when transferred to and subcultured in medium without interferon (dashed line in Fig. 1).

In a similar experiment, the "cure" was carried out by using 1,000 units of exogenous interferon per culture (Fig. 2). In this case, the "cure" was more rapid than with 200 units of added interferon; infective virus was not demonstrable in the medium after 7 days, and it took 14 days for infective centers in the L_{NDV} cell population to disappear.

It is puzzling why there is a requirement for relatively high concentrations of added exogenous interferon for prolonged periods of time to eliminate the persistent infection in the L cell-NDV system we have described. This requirement may be the result of some "protected" state of the viral genome in the persistently infected cells, or may be attributable to the refractoriness of such cells to interferon action.

It is interesting to note that Vilček and Stanček (4) reported that L cells persistently infected with tick-borne encephalitis virus were unresponsive to added exogenous interferon. Together with our results, their observations emphasize some of the problems which may be inherent in the use of interferon in the therapy of virus diseases, especially those which involve persistent viral infection of host cells.

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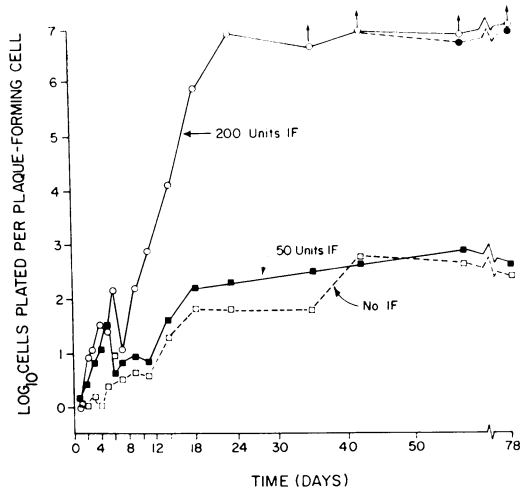


FIG. 1. Effect of continuous presence of exogenous added interferon (50 or 200 units per culture) on the frequency of infective centers in L cells persistently infected with Newcastle disease virus. (See text for details.)

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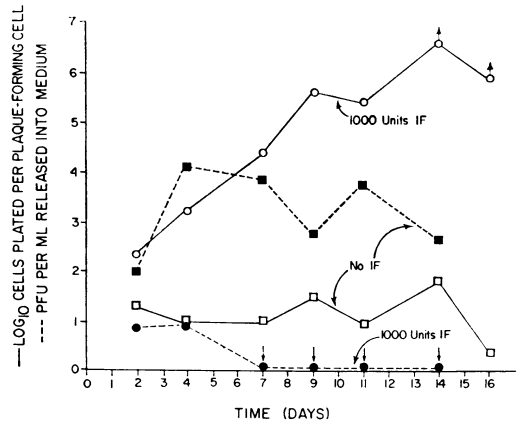


FIG. 2. Effect of continuous presence of exogenous added interferon (1,000 units per culture) on infective virus in the medium and on the frequency of infective centers in L cells persistently infected with Newcastle disease virus. (See text for details.)

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