Effect of Interferon Inducers and Interferon on Bacterial Infections

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The effect of interferon inducers and exogenous L-cell interferon on the infection of mice by Pasteurella tularensis or Diplococcus pneumoniae was investigated. The results indicate that the degree of protection is dependent on the type of inducer used. A variety of defense mechanisms with limited nonspecific activity appear to be involved.

There is increasing evidence that induction of interferon is not the only protective mechanism initiated by interferon inducers. Previous studies have shown that statolon, pyran, and endotoxin protected mice against Klebsiella pneumoniae (3) and have suggested that poly I:C protects against infection by gram-negative or gram-positive bacteria (5). Protection against bacterial infections cannot be explained by the generally accepted theory for the mechanism of action of interferon (2). Therefore, it is reasonable to assume that an additional biological property, resulting in protection against bacteria, is shared by these inducers. The present study was designed to determine whether this protection extends to other bacteria and whether the interferon inducers protect equally well against gram-positive and gram-negative organisms.

Groups of female Swiss albino mice (14 to 16 g) were treated with either Hanks balanced salt solution, poly I:C, statolon, pyran, tilorone, endotoxin, or L-cell interferon (two groups for each treatment). Twenty-four hours later, one-half of the mice in each group were challenged with Pasteurella tularensis while the others received Diplococcus pneumoniae. The mice were observed daily; no deaths were recorded after the 12th day. The results are shown in Tables 1 and 2.

Table 1 shows that, with P. tularensis as the challenge agent, pyran and endotoxin reduced the mortality rate whereas poly I:C, tilorone, and exogenous interferon had no effect. Statolon, on the other hand, increased the mortality rate. With the exception of endotoxin and statolon, each of the treatments resulted in an increase in the mean survival time. Endotoxin had no effect, whereas statolon treatment resulted in a shortening of the mean survival time. The relative mean survival rate, which gives an approximate but valuable overall evaluation of protection by taking into account both mortality and mean survival time (4), indicates that, with the exception of statolon, there was a protective effect in each instance. Statolon treatment, however, enhanced infection.

Table 2 shows the results obtained with D. pneumoniae. These data indicate that poly I:C, pyran, and endotoxin reduced the mortality rate and increased the mean survival time. Statolon reduced the mortality rate but had no effect on survival time. The relative mean survival rate indicated that poly I:C, statolon, pyran, and endotoxin protected against this agent, whereas tilorone and exogenous interferon had no effect.

These data show that prophylactic administration of interferon inducers can protect animals against experimental bacterial infections (both gram-positive and gram-negative organisms). The degree of protection is apparently dependent on the type of inducer used. The protection against extracellular organisms observed in this and other studies (3, 5) cannot be explained by the action of interferon. One must conclude then, that a different biological property is shared by these inducers which stimulates other defense mechanisms resulting in protection against bacterial infection. A different defense mechanism was apparently responsible for the protection against each of the organisms tested. This was shown by the ability of an inducer (tilorone, statolon) to protect against one organism but not the other. Those inducers that protected against both organisms stimulated both defense mechanisms. It is also apparent that the end result of inducer treatment is not always protection. There is often no effect or there can be a stimulation of the infectious process. The latter is clearly illustrated by statolon treatment which resulted in increased susceptibility to P. tularensis infection. Since statolon has been shown to pro-
protect mice against infection by K. pneumoniae (3), its deleterious effect is not a general phenomenon involving gram-negative organisms. A variety of defense mechanisms with limited nonspecific activity appear to be involved. Studies designed to identify these mechanisms are currently under way.

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**LITERATURE CITED**