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INTERFERON INDUCTION BY HUMAN ADENOVIRUS IN VIVO

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Summary. — Interferon production by chicks infected with adenovirus type 12 was studied. After intravenous injection, the formation of interferon in the serum proved to be biphasic. The "early" interferon production reached its maximum at 2—4 hours and the "late" interferon at 8—12 hours. Adenovirus type 12 treated with trypsin was capable only of stimulating the formation of the "late" interferon. Thus it is assumed that in vivo the trypsin-sensitive penton antigen is responsible for the induction of the "early" interferon.

The finding that the human adenoviruses are effective inducers in chick fibroblast cells (Béládi and Pusztai, 1967) promted us to study interferon induction by adenovirus type 12 in vivo. The virus propagated in HEp-2 cells was injected intravenously into 1—4 weeks old chicks. After inoculation of 0.5 ml of undiluted virus the chicks were bled at regular intervals and the blood samples from 3 animals killed at the same time were pooled. The presence of interferon in the serum was determined after heating at 56° C for 30 minutes on chicken embryo fibroblast monolayers by the plaque reduction method described previously (Béládi and Pusztai, 1967). Control chicks were inoculated with HEp-2 cells.

There were two distinct phases in the appearance of interferon in chick sera. The first detectable amounts appeared as early as 2 hours after infection. A further increase in interferon titre was usually observed at 3—4 hours and was followed by a decrease at 5—6 hours. A second peak of interferon occurred at 8—12 hours, but later again the level decreased. No detectable interferon could be demonstrated in the chick sera at 24 hours (Fig. 1).

Interferon production was not observed in the control chicks inoculated with HEp-2 cells.

Some physico-chemical and biological properties of the "early" interferon formed in chicks after inoculation with adenovirus type 12 were investigated with the following results:

Physico-chemical properties:

1. Trypsin treatment:
   1 mg/ml; 37° C; 1 hour — sensitive
2. Heat treatment:
   70° C, 1 hour — stable
   85° C, 1 hour — unstable

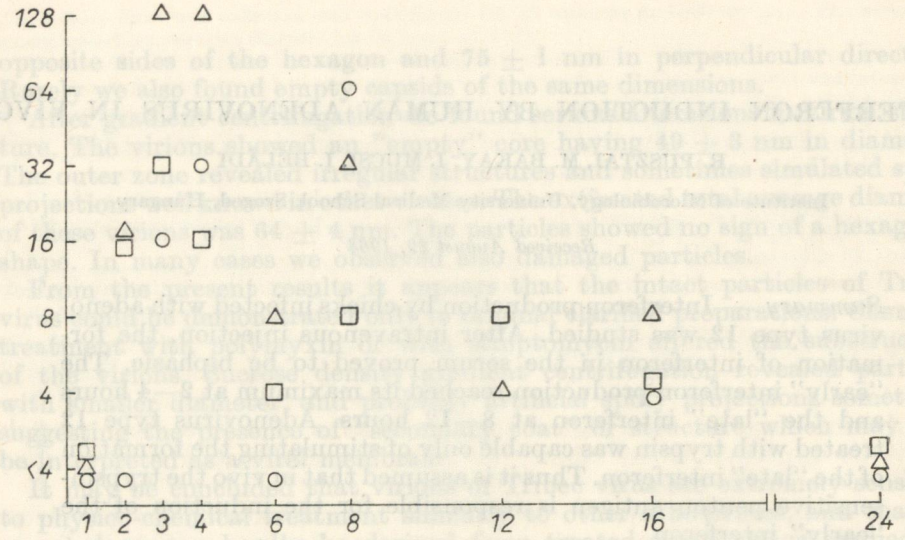

Fig. 1.

Interferon production in chicks inoculated with adenovirus type 12
The different symbols represent three individual experiments.
Abscissa: time in hours; ordinate: titre of interferon in serum (reciprocals).

Biological properties:

1. No direct effect on Sindbis virus.
2. Inhibitory effect against Sindbis, vesicular stomatitis and vaccinia viruses.
3. Actinomycin D inhibits its inhibitory effect.

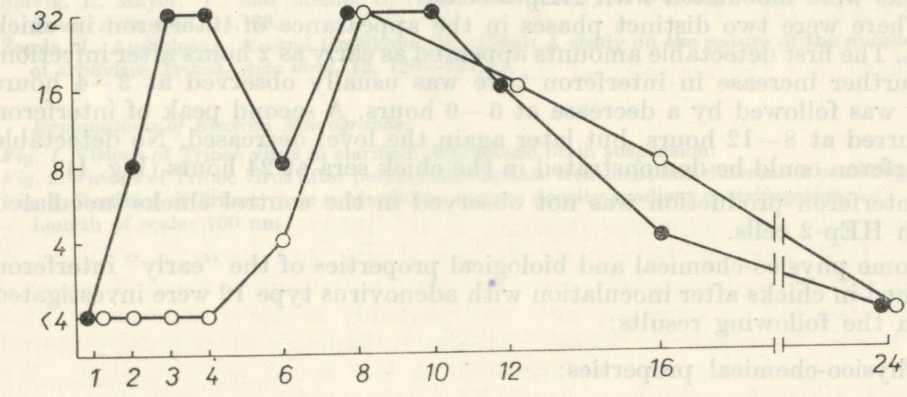

Fig. 2.

Interferon production in chicks after intravenous administration of trypsin-treated (○) and untreated (●) adenovirus type 12
Abscissa and ordinate as in Fig. 1.

These results show that the properties of the interferon were similar to those of interferons formed in chick cells inoculated with other viruses (Fantes, 1966).

It was previously found that, after trypsin treatment, the human adenoviruses — though still infective — are not able to stimulate interferon formation in vitro (Béládi and Pusztai, 1967). Thus the effect of trypsin treatment of virus on the formation of "early" and "late" interferon in vivo was now also investigated. In this case it was found (Fig. 2) that whereas the formation of "early" interferon was abolished there was no effect upon "late" interferon production.

The data obtained suggest that in vivo the trypsin-sensitive penton antigen is responsible for the induction of the "early" interferon. Experiments are in progress to test this assumption and to investigate whether "early" interferon production corresponds to the release of preformed interferon and whether de novo protein synthesis is only required for "late" interferon formation.

References

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