between the appearance of neurospecific proteins in nerve tissue culture and synaptogenesis [8]. It is also important to note that a study of the subcellular distribution of D antigen showed it to be predominantly localized in the synaptosomal fraction [3].

The results of the present investigation, together with data in the literature, thus indicate the important role of neurospecific D antigen in processes taking place in synapses. The dominant role in this phenomenon is perhaps played by FMC, the content of which is persistently higher than that of SMC of D antigen in the course of ontogeny.

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INDUCTION OF INTERFERON PRODUCTION BY DEXTRAN SULFATE

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It has recently been shown that dextran sulfate is a polyclonal stimulator of B lymphocytes [2]. Its ability to stimulate peripheral blood lymphocytes has been demonstrated [3]. The marked leukocyte-mobilizing activity of dextran sulfate is attributed to its possession of polyanionic properties. Certain polyanions are known to be able to induce interferon production in vertebrates.

The investigation described below was carried out to verify the interferon-inducing activity of dextran sulfate when administered by parenteral and enteral routes, and in the latter case its resistance to the action of enzymes of the gastrointestinal tract was noted. Certain other polyanionic substances also were investigated for the same purpose.

EXPERIMENTAL METHOD

Venezuelan equine encephalomyelitis virus strain 230 was used. The virus was subjected to passage through cell cultures. A continuous line of mouse cells L-929, obtained from the Tissue Culture Laboratory of the D. I. Ivanovskii Institute of Virology, Academy of Medical Sciences of the USSR, was used.

Noninbred albino mice weighing 10-12 g were used to induce interferon. To study the time

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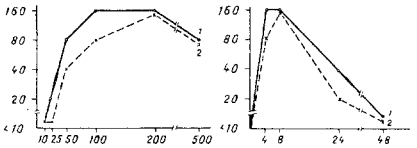

Fig. 1 Fig. 2

Fig. 1. Dependence of level of interferon production on dextran sulfate concentration. Abscissa, dose of dextran (in μg/mouse); ordinate, interferon titers (in Units/ml). 1) Intraperitoneal injection, 2) enteral administration of dextran.

Fig. 2. Time course of accumulation of interferon in blood serum of albino mice receiving dextran sulfate. Abscissa, time after administration of dextran (in h). Remainder of legend as to Fig. 1.

course of interferon production in the blood serum of the mice, 10 animals were taken at each stage of the experiments. Mouse blood sera were tested for interferon by microtitration on plastic plates. Serum interferon activity was determined by the usual method [1].

The following substances were used in the experiments: dextran sulfate, from Pharmacia, Sweden, with molecular weight of 500,000; native DNA, polyphosphate, polypentose, polyanethole sulfate, and heparin were obtained from the Institute of Medical Radiology, Academy of Medical Sciences of the USSR. All substances were dissolved in physiological saline and the appropriate dose was injected intravenously or given perorally in a volume of 0.2 ml.

EXPERIMENTAL RESULTS

Data on the level of interferon induction depending on the mode of administration and concentration of the dextran sulfate are summarized in Fig. 1. When the dextran was given by the parenteral and enteral routes, the maximal effect was produced by a dose of 200 μg/mouse (20 mg/kg). An increase in the dose to 500 μg/mouse was accompanied by some inhibition of interferon production.

The time course of induction of interferon after parenteral and enteral methods of administration also was similar (Fig. 2). Maximal interferon titers, reaching 160 Units/ml, were observed 4-8 h after administration of dextran sulfate. This was followed by a gradual fall in the interferon level, so that 24 h after administration of dextran it did not exceed 40 Units/ml.

The interferon induced by dextran sulfate was stable during changes in pH down to 2.0, but was inactivated after heating for 1 h at 56°C. Because of these findings, the interferon tested could not be classed as immune.

A study of the interferon-inducing activity of five other polyanionic preparations — native DNA, polyphosphate, polypentose, polyanethole sulfate, and heparin — showed that none of them was able to induce interferon production in mice.

The results thus demonstrate the ability of dextran sulfate to induce interferon formation when administered by parenteral and peroral routes. Until recently, only one inducer of interferon was known, namely, tilorone, which is active when administered enterally. All other preparations, including synthetic polynucleotides and natural double-stranded RNAs are active only when given parenterally. It is not yet clear which cells take part in interferon production in response to administration of dextran sulfate. It can be postulated that this is a function of enterocytes, considering their ability to produce interferon in response to the action of enteroviruses.

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