Thus the particular features of the local defensive reactions in the lungs in acute inflammation depend on the character of infection. In viral inflammation in the lung tissue, a decrease in the number of macrophages is found, together with an increase in their powers of attraction, and in the chemotaxic activity of the neutrophils. If a bacterial flora is present as well, the numbers of neutrophils, lymphocytes, and macrophages increase, and moderate hyperplasia of BALT develops. Functional activity of the lung phagocytes is characterized by weakening of chemotaxis of the neutrophils and strengthening of the phagocytic capacity of the macrophages. In the phase of convalescence the number of neutrophils decreases, the number of lymphocytes and macrophages remains high, and hyperplasia of BALT increases in severity. Functional activity of the phagocytes remains at higher levels than normally.

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ENZYME ACTIVITY OF THE INTERFERON SYSTEM IN VIRUS DISEASES

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The interferon system plays a definite role in resistance of the individual to viral infections on the first days of the disease and until the appearance of specific antibodies [9, 16, 17]. Many known viruses induce interferon in the body, and for that reason raised levels of circulating interferon are found in the blood in acute viral infections, but these quickly disappear. The antiviral action of interferon is due to activation of two enzymes in the cells, namely 2′,5′-adenylate svnthetase and a specific protein kinase [6, 8]. Since interferon-dependent enzymes have proved themselves to be stable markers of interferon action, their determination has come to be widely used in clinical studies [5, 11]. Activation of the enzymes has been demonstrated after injection of exogenous natural and recombinant interferons, after vaccination, and in acute virus diseases [10, 15]. Previously we studied the interferon status and activity of enzymes of the interferon system in individual virus diseases [1, 2]. In the investigation described below, changes in the enzymes in virus diseases of different etiology and with different clinical course has been compared for the first time: influenza, complicated by pneumonia, parainfluenza, chronic hepatitis B with delta-infection, and recurrent urticaria with frequent acute respiratory virus infection (ARVI) and herpes. Tests for interferon-dependent enzymes were used for the first time also to assess the effectiveness of treatment of virus diseases with recombinant α_2-interferon.

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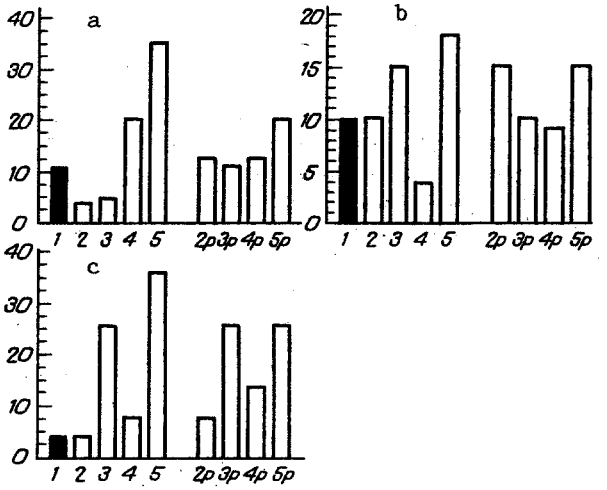

Fig. 1. Parameters of activity of the interferon system. Abscissa, healthy donors (1), patients with chronic active hepatitis B with delta-infection (2), with influenza complicated by pneumonia (3), with parainfluenza (9), with recurrent urticaria with frequent ARVI and herpes (5), after treatment with reaferon (2p, 3p, 4p, 5p). Ordinate, 2′,5′-adenylate synthetase activity (in pmoles/10^5 cells × 10), plasma protein kinase activity (in pmoles/100 μg × 10), and serum interferon activity (in U/ml). a) 2′,5′-Adenylate synthetase, b) plasma protein kinase, c) serum interferon. Schedule of reaferon treatment: inhalation in influenza and parainfluenza in a dose of 1 million 3 times a day intramuscularly or 600,000 4 times a day for 3-5 days, in chronic hepatitis B 1-3 million 2-3 times a week intramuscularly, in courses 1-3 months in duration; in recurrent urticaria 1 million on alternate days intramuscularly for 5 days.

EXPERIMENTAL METHOD

Patients with influenza, parainfluenza, and hepatitis B were admitted for treatment to the clinical department of the D. I. Ivanovskii Institute of Virology, and patients with recurrent urticaria were under observation at the Institute of Immunology, Ministry of Health of the USSR. The diagnosis of the infections, treatment with reaferon, and taking of blood from a vein were all carried out in the clinic. Normal human blood was obtained from the blood transfusion station. Fresh samples of blood with 100 U heparin were fractionated into leukocyte-enriched plasma and lymphocytes, which were purified in a Ficoll gradient. The samples were kept at —70°C. Enzymes from patients with virus infections and from healthy blood donors were determined in a single test in order to obtain comparable results. The techniques of determination of 2′,5′-adenylate synthetase and histone protein kinase activity were described by the writers previously [3]. The schedule of treatment with recombinant α_2-interferon (reaferon, Glavmikrobioprom, Moscow) is shown in Fig. 1. The serum interferon titer was determined by a micromethod on human fibroblasts (line M19), on the basis of inhibition of the cytopathic action of vesicular stomatitis virus.

EXPERIMENTAL RESULTS

The results of comparative determination of 2′,5′-oligoadenylate synthetase activity in lymphocytes, of histone protein kinase in the plasma, and of circulating interferon in the serum in patients with influenza, parainfluenza, hepatitis B, and urticaria with frequent ARVI and herpes are given in Fig. 1. Parameters of the interferon system clearly deviated considerably from the norm (healthy blood donors). In patients with recurrent urticaria and frequent ARVI and herpes, activity of the enzymes and serum interferon were above normal. Conversely, in chronic active hepatitis B with delta-in-

fection and severe forms of influenza with pneumonia, levels of 2′,5′-adenylate synthetase activity were low. Plasma protein kinase activity was depressed in parainfluenza, although in patients with other infectious diseases protein kinase activity was increased This variability of the results can evidently be explained by differences in the course of the infectious process and in the mechanisms of the antiviral action of interferon on different viruses [9, 14]. Furthermore, there are two independent ways of realization of antiviral action: activation of 2′,5′-adenylate synthetase, accumulation of 2′,5′-adenylate products in the infected cells, and activation of endogenous RNase L by them, and local degradation of single-helical forms of viral RNA [6, 8]; activation of dsRNA-dependent protein kinase, phosphorylating the translation initiation factor EIF-2, leading to the appearance of translation in virus-infected cells [7, 8]. Some viruses, in certain cell systems, are resistant to the action of interferon (influenza and herpes viruses, for example). To exhibit an antiviral effect, the presence of the Mx gene, activating interferon, is essential [4]. Other viruses (adenovirus, vaccinia virus) form products during replication which inactivate enzymes of the interferon system [12, 15]. In vivo, the immunity system additionally has some influence on realization of the antiviral action of interferon [18].

Thus in virus diseases of varied etiology pathological changes take place in the interferon system. According to our data, these changes can be corrected by administration of exogenous recombinant interferon, which is not only an activator of interferon-dependent enzymes, but also a physiological regulator in the case of pathological activation (recurrent urticaria) (Fig. 1)

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