# Functional Activity of Neutrophilic Granulocytes in Patients with Relapsing Herpes

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Neutrophilic granulocytes exhibit different degrees of functional activity in patients with relapsing herpetic infection in various phases of the disease. A high level of myeloperoxidase is detected in the serum over the entire course of the disease and a three-fold increase of serum lactoferrin appears at the beginning of remission.

**Key Words:** *relapsing herpetic infection; neutrophilic granulocytes; lactoferrin; myeloperoxidase; nonspecific resistance*

The agent of relapsing of herpetic infection, *herpes simplex* virus, is characterized by an antigenic diversity, pantropism, and lifelong persistence in the host organism, probably in association with spinal ganglion cells and immunocytes. The fine structure of *herpes simplex* virus has been studied in detail but the mechanisms of its persistence and the causes of relapses are unknown. A pivotal role in antiviral protection is assigned to cell-mediated immune mechanisms [1,2]. Recently, factors of nonspecific resistance and their participation in the array of responses of the organism to viral infection have attracted increasing interest. As is shown by the immunoperoxidase method [6], the content of lactoferrin falls in neutrophilic granulocytes (NG) in viral infections. The present investigation was undertaken to examine the functional activity of NG in relapsing viral infection on the assumption that NG, which perform key functions in the inflammatory reaction and possess a powerful antimicrobial potential, have a role to play both in protecting the organism from the virus and in establishing the relapsing course of the disease.

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## MATERIALS AND METHODS

The diagnosis of relapsing herpetic infection was made from the clinical and anamnestic data and confirmed by the isolation of *herpes simplex* virus in cell cultures, by the complement fixation test, and by the fluorescing antibody method. The nonspecific cellular reactions were assessed by the functional activity of neutrophils determined by phagocytosis, the nitroblue tetrasolium (NBT) test, and the lysosomal-cation test. Cationic lactoferrin proteins and myeloperoxidase were determined in the serum by immunoenzyme assay. The level of serum immine complexes was measured routinely.

## RESULTS

Twenty-seven patients of both sexes with relapsing herpetic infection aged from 15 to 53 years were observed for 3 years. All patients exhibited a severe course of infection with 5-12 flare-ups per year lasting 10-14 days. They were repeatedly examined both in exacerbation and in remission. Clinical observation revealed the following morphological phases in the infection: phase I: the appearance of vesicles, phase II: the development of erosions, phase III: of crusts, and phase IV: the absence of inflammatory changes. Clinically phases I and II corresponded to exacerbation, phase IV to remission, and phase III was considered as intermediate.

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**TABLE 1.** Parameters of Lactoferrin and Myeloperoxidase in Serum of Patients with Chronic Relapsing Herpetic Infection in Different Phases of the Disease

| Parameter | Norm | Phase | | | |
|---|---|---|---|---|---|
| | | I | II | III | IV |
| Lysosomal–cation test, arb. units | 1.58±0.01 | 1.26±0.064** | 1.44±0.028* | 1.44±0.039* | 1.56±0.027 |
| Myeloperoxidase, ng/ml | 160±20.0 | 360±71.7*** | 351±39.1*** | 318±39.0*** | 431±44.0*** |
| Lactoferrin, ng/ml | 1000±140.0 | 731±134.1 | 1392±142.6** | 1542±186.2** | 2282±216.9*** |

Note. *$p<0.05$, **$p<0.01$, ***$p<0.0005$ as compared to the norm.

The maximal content of immune complexes is noted in the serum in phase IV (117±7.6) and the minimal content in phase II (90±10.0, $p<0.05$). The determination of NG functional activity brought out some regularities. Patients in phase III exhibited maximal NG phagocytosis (51±2.1, $p<0.05$), while on the contrary, the index of NBT-test activity was minimal (0.4±0.07, $p<0.05$). Against the background of relatively high NG phagocytosis (which, however, remained within normal values), a very high NBT index was revealed in phase I (5.5±4.36). The content of cationic proteins in NG (Table 1), determined by the lysosomal-cation test, was minimal in phase I ($p<0.05$), rose in phases II and III, though remaining substantially below the norm ($p<0.01$), and, finally, in phase IV, did not differ from that seen in healthy individuals of this age. The serum content of myeloperoxidase, regardless of the phase of disease, exceeded the normal value twofold. The concentration of lactoferrin in the serum was somewhat below normal in phase I but then (phases II-IV) rose considerably, attaining maximal values in the stage of remission (phase IV) ($p<0.0005$).

It is known that cationic proteins contained in NG granules perform various functions in an inflammatory reaction (inflammatory mediators, nonspecific opsonins in phagocytosis, modulators of blood coagulation and fibrinolysis, and so on). Cationic proteins impart antimicrobial potential to NG due to their complex influence on the structure and metabolism of microorganisms [4,5]. We discovered that the acute phase of the disease (phase I) corresponds to a fall of the total content of cationic proteins detected in the lysosomal-cation test, which attests to intensive secretion of NG and active involvement of these cells in the protection of the organism. The positive dynamics of the infectious process is attended by an elevation of the level of cationic proteins and restoration of the lysosomal-cation test to normal values.

However, the high level of serum myeloperoxidase during the entire cycle of the disease attests to the constant vigorous secretion of NG, probably due to accelerated renewal of the blood pool of these cells. The NBT-test parameters also indicate the active involvement of NG in the pathological process, which results in the attenuation of their functions in phase III.

Lactoferrin plays an important role in the cell-to-cell cooperation of immunocytes. Its receptors are found on monocytes, macrophages, NG, activated T lymphocytes, and B lymphocytes [8]. Lactoferrin absorption by mononuclear phagocytes inhibits their capacity to form hydroxyl radical and protects cells from autoperoxidation of the membrane [7]. An elevated level of serum lactoferrin may be viewed as antioxidant protection realized by NG and as a favorable prognostic sign of remission. Lactoferrin is also a marker of specific NG granules carrying a set of receptors on their inner membrane [3]. Its release from specific granules is accompanied by the installation of receptor proteins in the outer NG membrane, which may lead to an increase of NG functional activity and subsequent activation of the mononuclear phagocyte system, which destroys the infectious agent [4]. However, we found a stepped-up level of immune complexes in remission, attesting to the defectiveness of mononuclear phagocytes probably due to the tropism of *herpes simplex* virus toward these cells. Thus, the debility of effector cells is observed in exacerbation and in remission, which in this case is an unstable balance between host organism and pathogen, when the potencies for the next cycle of the disease are accumulated.

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