

Biorhythms of Functional Activity of Phagocytes in Iron Deficiency

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Biorhythms of absorption capacity of neutrophils and monocytes were studied in women with latent iron deficiency. We revealed disorders in circadian organization of the mononuclear phagocyte system and decreased reserve capacity of nonspecific organism's resistance against the background of tissue iron deficiency. Informative value of desynchronization in circadian structure of the phagocyte absorption capacity as the early marker of prelatent iron deficiency was established.

Key Words: *iron deficiency; neutrophils; monocytes; phagocytosis; biorhythms*

Iron deficiency anemia (IDA) accounts for about 80% anemias. According to WHO data, about 200 million peoples suffer from iron deficiency (ID). Infants and women of reproductive age are the most vulnerable for ID. Manifest stage of ID, *i.e.* exhaustion of hemoglobin pool or IDA, is preceded by depletion of the reserve, tissue, and transport iron pools, which corresponds to prelatent and latent forms of ID.

ID is associated with not only hypoxia, but also decreased organism's resistance to infection [3]. Functional deficiency of immunocompetent cells and phagocytes due to deficiency of iron-dependent enzymes [6,8], defects of cell receptor system modification [11] and intracellular metabolism [10], and disturbances in cell-cell interactions [12,14] underlie congenital and acquired immunodeficiency in ID. Macrophages, central elements of the immune response and the phagocytic system [5,7,13], play an important role in the regulation of iron metabolism [1,2]. Therefore their integrative function in the formation of the basal level of body reactivity in ID is impaired.

We elucidated the mechanisms and biorhythmological criteria of immunosuppression in latent ID.

MATERIALS AND METHODS

Nonpregnant women (148 healthy and 33 with latent ID) aged 19-25 years were examined during the early luteal phase of the menstrual cycle.

Blood was collected from the ulnar vein and stabilized with heparin (500 U was dissolved in 5 ml saline). The measurements were repeated 4 times over 24 h: at 6.00, 12.00, 18.00, and 24.00.

Latent ID was diagnosed on the basis of disorders in circadian rhythm of sideremia, decreased serum ferritin, and increased total iron-binding capacity of the serum against the background of normal erythrocyte and hemoglobin content in the peripheral blood. The total and differential leukocyte counts were evaluated routinely. Absorption capacity of peripheral blood neutrophils and monocytes was evaluated by phagocytosis of 0.9- μ latex particles. Pyrogenal was used as the stimulator. The phagocytic index (PI) and phagocytic number (PN) were estimated in blood smears per 50 neutrophils and 10 monocytes. Coefficient of activation was calculated as the ratio of stimulated to spontaneous activities. The data were processed using Student's *t* test.

RESULTS

In women with ID the mean circadian PI of neutrophils and monocytes increased, while PN decreased

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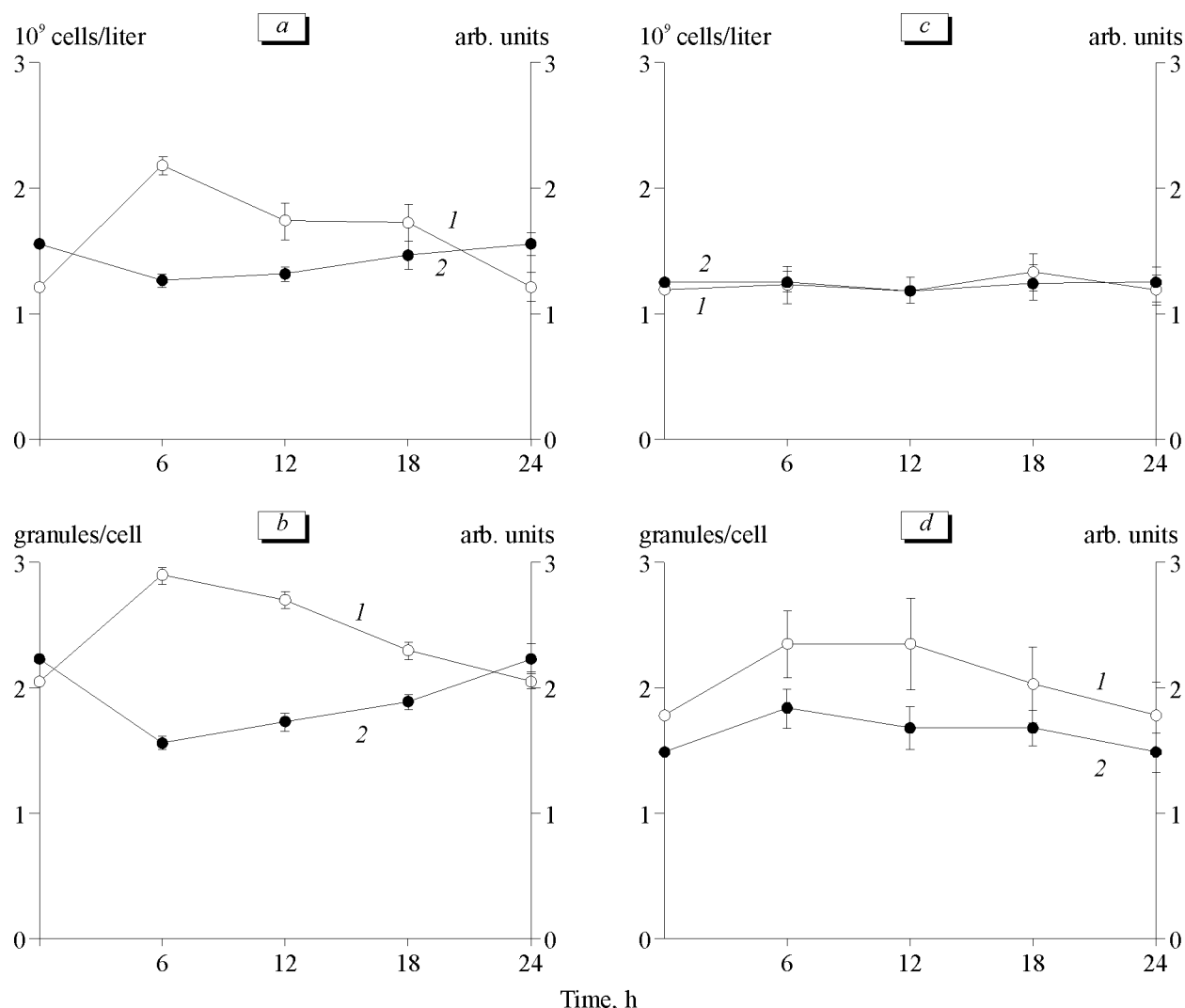


Fig. 1. Circadian dynamics of neutrophil phagocytic index (a, c) and phagocytic number (b, d) (1, left ordinates) and activation coefficients (2, right ordinates) in healthy women (a, b) and patients with latent iron deficiency (c, d).

(Figs. 1, 2). The mean coefficients of activation for monocyte PI and neutrophil PN increased and those of neutrophil PI and monocyte PN decreased.

Analysis of circadian rhythms of neutrophil and monocyte absorption capacity revealed early signs of imbalance in the phagocytic system in ID: changes in counterphase relationships between spontaneous and induced parameters characteristic of healthy women (Figs. 1, 2) and desynchronization of circadian rhythms of neutrophil and monocyte absorption activity. Disappearance of counterphase relationships between circadian dynamics of spontaneous and induced tests in ID indicates reduced reserve capacity of phagocytes.

Decreased functional activity of micro- and macrophages under conditions of tissue iron depletion in prelatent and latent ID determines impaired organism's resistance to infection. Analysis of patient's histories showed that 42% pregnant patients with IDA had chro-

nic inflammations: 27% had pyelonephritis and glomerulonephritis, 4% cholecystitis, and 11% suffered from gastritis with low secretory activity. It is known that 61% atrophic gastritis in patients with IDA are associated with *Helicobacter pylori* infection [13], which, in turn, promotes further progress of ID. During pregnancy 15% women with IDA had acute respiratory viral infections.

Hence, the presence of chronic inflammatory diseases should be regarded as a manifestation of immune dysfunction, which can result from latent ID.

Therefore, imbalance in the phagocytic system decreasing its reserve capacities is the early sign of ID. Modification of the temporal organization of the cell immunity changes optimal morphofunctional relationships essential for the realization of immune functions. Dysregulation of leukocyte phagocytic activity and immune mechanisms is most likely the leading cause of chronization of inflammatory processes in ID [4].

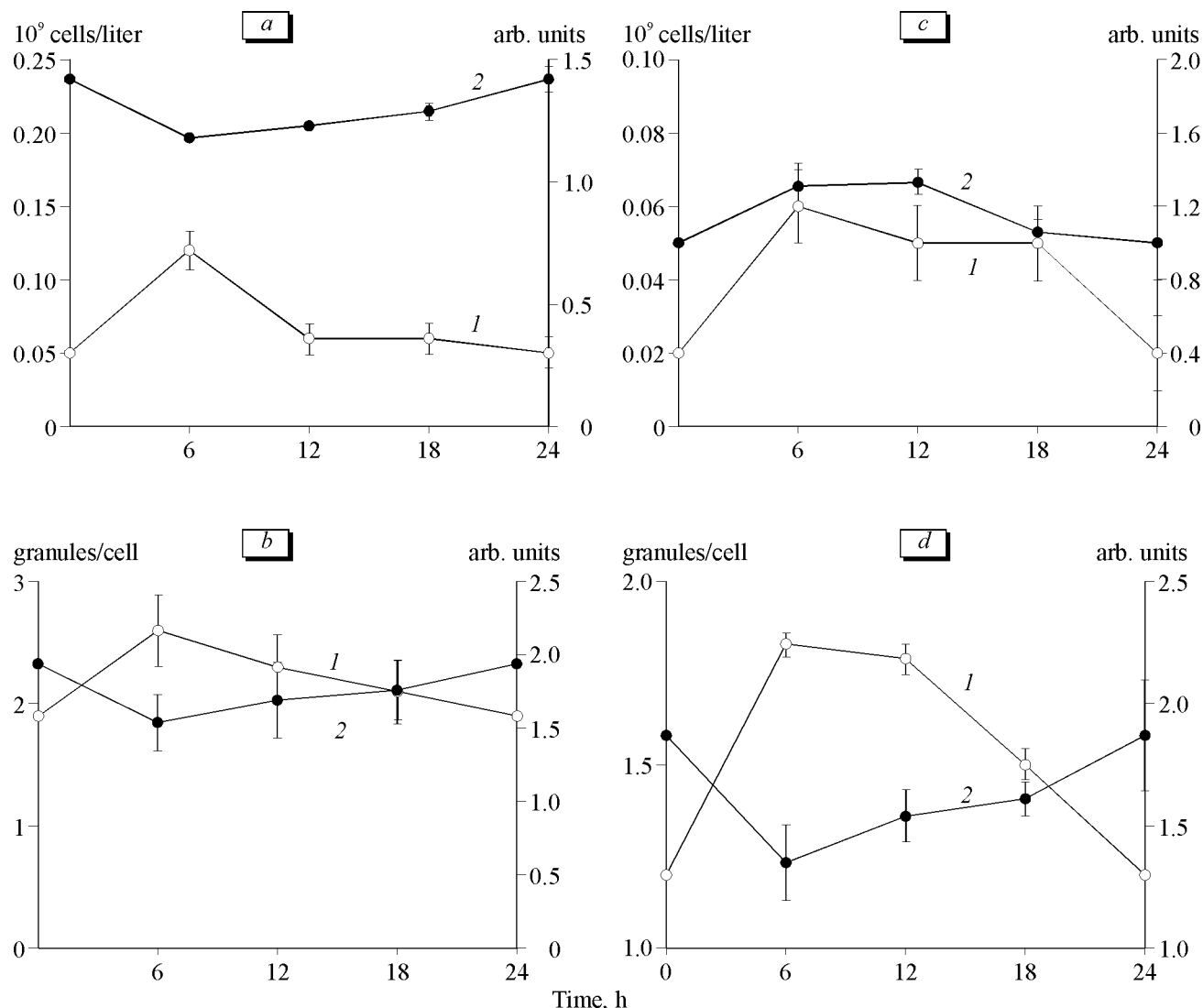


Fig. 2. Circadian dynamics of monocyte phagocytic index (a, c) and phagocytic number (b, d) (1, left ordinates) and activation coefficients (2, right ordinates) in healthy women (a, b) and patients with latent iron deficiency (c, d).

Changes in the absolute values of immune parameters are preceded by disorders in the rhythmic structure of the phagocytic system.

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