CYTOLOGICAL COMPOSITION OF LYMPH DURING THE FEBRILE REACTION

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The role of the lymphatic system in the formation, utilization, and redistribution of cells during the febrile reaction (FR) has remained completely unstudied, although the cytological composition of lymph is known to be an integral parameter of the functional state of lymphoid tissue, largely predetermining the specific and nonspecific resistance of the individual during the development of pathology. The lymphatic system also resorbs, stores, and transports the cellular contents into the blood stream, rendering them harmless and "analyzing" them in the lymph nodes. We may consider that the study of the cytological composition of lymph during FR is of definite interest within the context of improving our knowledge of the pathogenesis of this typical pathological process and the role of the lymphatic system in "cellular homeostasis" of the body fluids during fever.

In the investigation described below the cytological composition of lymph from the thoracic lymph duct (TLD) of rabbits was investigated during an FR of varied duration.

EXPERIMENTAL METHOD

Experiments were carried out on 49 adult chinchilla rabbits weighing 2.5-4.2 kg. The FR was reproduced as in [9]. As the control, animals receiving injections of pyrogen-free physiological saline, made up in bidistilled water, were used. Lymph was obtained from TLD at the point where it empties into the venous angle. The total number of leukocytes in the lymph was counted in a Goryaev counting chamber [10]. For the differential cell count, films of lymph were stained by the Romanovsky—Giemsa method. The experimental results were subjected to statistical analysis. The animals were killed by injection of a lethal dose of the general anesthetic.

EXPERIMENTAL RESULTS

As the investigations showed (Table 1), the cellular composition of lymph from TLP of normal rabbits consists mainly of small and medium-sized lymphocytes.

The FR was accompanied by quantitative and qualitative changes in the cytological composition of the TLD lymph. After a single injection of pyrogenal, at the stage of the rise of body temperature (2.5-3 h after the beginning of injection of pyrogenal) a decrease was observed in the number of leukocytes, to be replaced at the stage of the temperature drop by a tendency to increase. In the initial stage of fever there was also an increase in the number of eosinophils in the lymph, whereas 5-5.5 h after injection of pyrogenal, an increase in the relative percentage of prolymphocytes was added to these changes.

After three injections of pyrogenal, leukocytosis developed in the lymph, with an increase in the number of eosinophils and prolymphocytes and a decrease in the number of small and medium lymphocytes.

Prolonged (5 and 10 days) fever was accompanied by more marked changes in the cytological composition of the TLD lymph: an increase in the number of leukocytes, a decrease in the number of small and medium lymphocytes, and an increase in the number of undifferentiated cells — blast cells, large lymphocytes, prolymphocytes. By the 10th day after the fifth injection of pyrogenal the number of leukocytes in lymph from the rabbit TLD showed a decrease, and of the undifferentiated cells, only the number of prolymphocytes remained increased.

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TABLE 1. Cytological Composition of Lymph from Thoracic Lymph Duct of Rabbits during Febrile Reaction (M ± m)

Parameter	Control	Number of injections of pyrogenal					
		1		3	5		10
		after 2.5-3 h	after 5-5.5 h	4th day	6th day	10th day	11th day
Number of leukocytes in 1 µl lymph	11506,12	9780,43**	13360,57	13862,43**	16946,14*	9302,14**	15195,71*
	844,07	400,31	1054,15	923,35	791,83	603,55	613,00
Small and medium lymphocytes, per cent	93,60	93,20	91,23	91,03**	84,31*	91,91	83,91*
	0,47	0,94	0,71	1,17	1,13	1,23	1,14
Large lymphocytes, per cent	4,63	3,91	5,17	5,06	7,80*	4,40	7,71*
	0,31	0,56	0,39	0,50	0,54	0,64	0,45
Prolymphocytes, per cent	0,93	1,51	2,06***	2,37***	4,37*	2,17**	4,60*
	0,22	0,47	0,36.	0,46	0,49	0,56	0,69
Blast forms, per cent	0,18	0,26	0,23	0,31	1,97*	0,23	2,49*
	0,04	0,08	0,05	0,10	0,24	0,08	0,18
Eosinophils, per cent	0,68	1,20**	1,31**	1,23**	1,26**	1,29**	1,29**
	0,17	0,13	0,17	0,30	0,20	0,21	0,18

Legend. In each group n = 7; *p < 0.001, **p < 0.05, *** p < 0.02.

It will be noted that the physiological activity of the lymphoid system is constructed according to the repopulation principle, based on feedback, as expressed by continuous migration of lymphocytes from one lymphoid organ to another and from one tissue to another [5]. On the basis of data relating to activation of the hypothalamo-hypophyseo-adrenal system and elevation of the blood corticosteroid level during FR [1, 6], the decrease in the number of lymphocytes in the lymph during the first hours of development of fever can be explained, in our view, by the following mechanisms. We know that the number of circulating lymphocytes is inversely proportional to adrenocortical functional activity. Increased secretion in the adrenal cortex or administration of exogenous glucocorticoids (GC) gives rise to lymphocytopenia, with inhibition of lymphocyte recirculation at the lymph node level [7]. Meanwhile, other processes involved in the mechanism of the developing lymphocytopenia include inhibition of proliferation of lymphocytes and their lysis, i.e., involution of the lymphoid tissues takes place under the influence of GC [3, 11].

In our view the decrease in the number of lymphocytes in the lymph of TLD in these experiments was largely due to the effect of GC on migration and recirculation of the lymphocytes and retention of lymphocytes in the tissues, especially lymphoid tissue. The mechanism of action of GC on the processes of recirculation of the lymphoid cells is connected, on the one hand, with decreased permeability of the endothelium of the postcapillary venules of the lymph nodes, leading to obstruction of lymphocyte migration from the blood into the lymphoid tissue [14]. On the other hand, GC can act through the enzyme adenylate cyclase on the membrane surface of the lymphocytes, to make it more adhesive, and this leads to inhibition of lymphocyte recirculation in the body [12, 15].

The lymphocytological action of GC could not be completely ruled out in our experiments, but probably it cannot take place because the small and medium lymphocytes of the circulating pool, most of which consist of T-cells [13], are particularly sensitive to their action.

At the same time, we know that the lymphocytopenia developing in response to injection of GC is evidence of lymphocyte migration from lymphoid tissue into the blood and into other organs, especially bone marrow. Lymphocytes which have migrated into the bone marrow induce activation of hematopoiesis [3]. It has been suggested that lymphocyte migration also is due to an increase in tone of the sympathetic nervous system and to the release of large quantities of catecholamines into the blood stream [2, 3]. Meanwhile, during FR the sympathicoadrenal system is activated and catecholamines are released [4]. On the basis of the above accounts there is good reason to suppose that because of activation of hematopoiesis during FR the lymphcytopenia is followed by an increase in the number of lymphocytes, and also an increase in the relative percentage of young cells, such as prolymphocytes and blast cells in the lymph.

Of the cells of the granulocytic series in the lymph, those found most frequently are eosinophilic leukocytes. The increase in the relative percentage of eosinophils during fever is evidently connected with their rapid elution from the lymphatic tissue, as the cells bound least strongly to the lymph node tissue. On the whole, migration of eosinophils from lymphoid tissue into the blood stream during FR is probably an expression of a protective reaction, for eosinophils have the ability to adsorb biologically active substances, the concentration of which, as we have shown, is increased in the lymph and blood [8].

In the late stages after five injections of pyrogenal, the reduction in the number of lymphocytes in the TLD lymph evidently takes place as a result of functional exhaustion of the lymphoid tissue, and it is also connected with qualitative disturbances of the lymphocytes themselves: a decrease in the intensity of RNA synthesis or a change in the properties of their membrane surface, which may make the outflow of lymphocytes into the extravascular lymphoid tissues more difficult or may slow their passage into the lymphoid organs along the path of recirculation dramatically.

Thus the lymphatic system plays a leading role in the mobilization of lymphoid cells during PR, which is expressed as the migration of large numbers of lymphocytes through the TLD into the blood stream.

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