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# CHANGES IN DEPENDENCE OF LYMPHOCYTE REACTIVITY TO PHYTOMITOGENS ON ENDOGENOUS HORMONAL FACTORS IN EXPERIMENTAL BACTERIAL PROSTATITIS

V. P. Chernyshov, L. P. Imshinetskaya,  
N. D. Tron'ko, V. N. Demchenko,  
T. I. Peretyatko, and V. L. Chaikovskaya

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Dependence of lymphocyte blast transformation reactions (BTR) on phytohemagglutinin P, concanavalin A, and the mitogen pokeweed on the plasma 11-hydroxycorticosteroid (11-HCS) and testosterone (T) levels and the urinary excretion of 17-ketosteroids was studied in 11 dogs with experimental urogenic (urethrogenic) prostatitis produced by means of a pathogenic staphylococcus isolated from a patient with chronic prostatitis. Before the experiment, multiple correlation was found between hormonal factors and BTR indices, but this was upset 1 month after infection of the animals and restored 2 months after infection. Before the experiment the association was expressed mainly by direct correlation with 11-HCS, but 2 months after the experiment, by negative correlation with T. The homeostatic character of the hormonal-lymphoid dependence relative to T is suggested.

KEY WORDS: reactivity of lymphocytes; endogenous hormonal factors; experimental prostatitis.

When androgenic saturation of the body is reduced, direct correlation is found between the indices of the lymphocyte blast transformation reaction (BTR) to phytohemagglutinin P (PHA) and testosterone (T) excretion in patients with chronic prostatitis and sterility [4]. On the other hand, castration of healthy animals can increase the immune response as a result of an increase in the number of T lymphocytes [5]. Exogenous T in vitro depresses the reactivity of normal lymphocytes to PHA [1, 9, 11]. Conflicting results have been obtained in the study of correlation between the circadian rhythm of the cortisol level and BTR to PHA in the healthy organism [8, 10].

The object of the present investigation was to study the dependence of lymphocyte reactivity on hormonal factors by the use of a model of an isolated bacterial affection of an androgen-dependent organ – the prostate. Considering that the body is a multiple-factor self-regulating system in which the resultant effect on the lymphoid system is exerted by a combination of hormonal factors, dependence of the BTR indices to PHA, to concanavalin A (con A), and to pokeweed mitogen (PWM) on the plasma 11-hydroxycorticosterone (11-HCS) and T levels and of the urinary excretion of 17-ketosteroids (17-CS), reflecting the activity of T metabolism, was estimated.

## EXPERIMENTAL METHOD

Experiments were carried out on 11 young sexually mature male dogs in which an isolated urogenic (urethrogenic) bacterial prostatitis was produced by the methods described previously [2], by infection with

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TABLE 1. Values of BTR to Phytomitogens and Hormonal Levels (11-HCS, T, 17-CS) in Experimental Urogenic (urethrogenic) Prostatitis (n = 11, M ± m)

Index	Time of testing			
	before experiments	1 month	1.5 months	2 months
PHA, %:				
BS	70,5±1,1	53,8±2,1 †	53,8±3,3 †	59,0±3,1*
Auto	69,0±1,2	52,4±2,6 †	52,3±3,5 †	59,3±2,9*
Con A, %:				
BS	72,6±0,9	54,7±2,3 †	56,1±3,7 †	64,3±2,6*
Auto	70,9±0,8	52,0±2,0 †	55,3±3,6 †	63,4±3,1*
PWM, %:				
BS	71,5±1,1	53,0±2,6 †	56,0±3,7 †	63,7±2,9 †
Auto	69,8±1,1	52,6±2,8 †	54,3±3,8 †	61,3±2,9*
Blood 11-HCS, µg %	6,79±1,17	7,47±1,08	6,38±0,75	3,43±0,72*
Blood T, ng %	87,5±17,7	255,9±29,0 †	183,0±23,9 †	147,2±27,9
Urinary 17-CS, mg/day	0,75±0,13	0,87±0,13	0,89±0,14	1,00±0,16

**Legend.** Here and in Table 2: auto) culture in BTR with autologous serum, BS) with bovine serum. Significance of difference from initial level: \*) P < 0.05, †) P < 0.01.

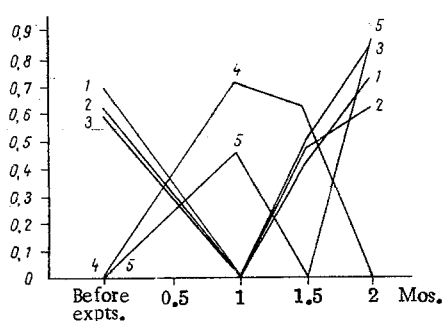


Fig. 1

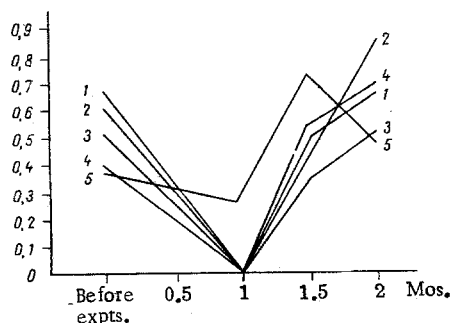


Fig. 2

Fig. 1. Experimental prostatitis. Change in coefficients of multiple correlation for linear model of the type  $y=f(11\text{-HCS}, T, 17\text{-CS})$ , where  $y$  is the BTR index during culture of lymphocytes with bovine serum. 1)  $y_1$  (con A); 2)  $y_2$  (PWM); 3)  $y_3$  (PHA); 4)  $y_4$  (without mitogen); 5)  $y_5$  (PHA/con A).

Fig. 2. Experimental prostatitis. Changes in coefficients of multiple correlation for linear model of the type  $y=f(11\text{-HCS}, T, 17\text{-CS})$ , where  $y$  is the BTR index during culture of lymphocytes with autologous serum. 1)  $y_6$  (PHA); 2)  $y_7$  (con A); 3)  $y_8$  (PHA-stimulated lymphocytes); 4)  $y_9$  (PWM); 5)  $y_{10}$  (PHA-blast cells).

a pathogenic strain of *Staphylococcus aureus*, isolated from the prostatic secretion of a man with prostatitis, in a dose of 1.5 billion bacterial cells. This strain was found in the prostate tissue at the end of the experiment (2 months). No bacteria could be seeded from the blood at any time during the experiments. For the BTR test peripheral blood lymphocytes of the dogs were cultured in medium 199 in two variants: with the addition of 20% bovine serum and with autologous serum [3]. The following phytomitogens were used: PHA P from Difco, con A from Sigma, and PWM from GIBCO, in a dose of 5 µg/ml. The incubation time was 72 h. The total number of stimulated lymphocytes and blast cells was determined in per cent. The plasma 11-HCS [6] and T levels were studied by a radioimmunologic method using "Testox" kits from CEA-Fra-Sorin, according to the instructions supplied. Radioactivity was determined with an Isocap-300 (USA) scintillation counter. The 24-hourly excretion of total 17-CS with the urine was determined as in [7]. The results were subjected to statistical analysis on the Minsk-22 computer.

## EXPERIMENTAL RESULTS

The immunologic and hormonal indices in the course of development of bacterial prostatitis are shown in Table 1. The reactivity of the lymphocytes fell after 1 month. By 2 months a tendency toward recovery was observed, although the indices were still below their initial values. Spontaneous lymphocyte transformation did not change significantly in the course of the experiment. By 2 months the 11-HCS level was signifi-

TABLE 2. Dependence of Indices of BTR to PHA, Con A, and PWM on hormone (11-HCS, T, 17-CS) Levels during Development of Experimental Urogenic (urethrogenic) Prostatitis

Mitogen	Time of investigation	Coefficients of correlation							
		culture with bovine serum				culture with autologous serum			
		multiple correlation-R (11-HCS, T, 17-CS)	paired correlation ( $r_{xy}$ )			multiple correlation-R (11-HCS, T, 17-CS)	paired correlation ( $r_{xy}$ )		
			11-HCS	T	17-CS		11-HCS	T	17-CS
PHA	Before experiment	0.64*	+0.57	+0.28	-0.32	0.67*	0.60*	0.34	-0.19
	1 month after experiment	0	+0.06	-0.10	+0.08	0	0.01	-0.13	-0.05
	1.5 months after experiment	0.49	-0.43	-0.49	+0.47	0.49	-0.45	-0.51	0.46
	2 " " " "	0.85†	-0.43	-0.74†	+0.45	0.66*	-0.32	-0.63*	0.43
Con A	Before experiment	0.69*	+0.55	+0.32	-0.36	0.60*	0.59	0.18	-0.32
	1 month after experiment	0	-0.16	-0.19	-0.005	0	0.05	-0.17	0.27
	1.5 months after experiment	0.42	-0.40	-0.42	+0.49	0.43	-0.41	-0.46	0.47
	2 " " " "	0.74†	-0.43	-0.69*	+0.38	0.83†	-0.44	-0.72†	0.45
PWM	Before experiment	0.63*	+0.34	+0.36	-0.49	0.39	0.31	0.32	-0.36
	1 month after experiment	0.12	+0.47	+0.02	-0.25	0	-0.01	-0.21	-0.01
	1.5 months after experiment	0.49	-0.47	-0.61	+0.31	0.54	-0.47	-0.58	0.42
	2 " " " "	0.62*	-0.43	-0.57	+0.42	0.69*	-0.46	-0.59	0.46

cantly lowered, whereas the T level had fallen after a considerable initial rise, but was still higher than initially. According to the character of the change in 17-CS excretion two groups of animals could be distinguished. Those with high initial indices (above 0.9 mg/day) responded with a decrease, those with low initial indices (below 0.9 mg/day) responded with an increase in hormone excretion.

The dependence of lymphocyte reactivity on the level of the hormones studied was assessed by the coefficient of multiple correlation R as a function of time for a linear model of the type  $y=f(17\text{-CS}, T-11\text{-HCS})$ , where y is a variable corresponding to the values of BTR (Figs. 1 and 2). In intact dogs (before the experiment) significant correlation was found between the BTR values and the 11-HCS, T, and 17-CS levels taken together. Values of the coefficient of paired correlation ( $r_{xy}$ ) show that this association was due mainly to direct correlation with 11-HCS and to a lesser degree with T, and to negative correlation with 17-CS (Table 2). After 1 month multiple correlation was disturbed, but restored after 2 months. However, all values of  $r_{xy}$  changed to the opposite sign. Negative correlation with T was most significant ( $P < 0.01$ ). Correlation with the indices for blast cells and stimulated lymphocytes separately was not significant at any time during the experiments. Correlation between BTR PHA/con A (bovine serum) values with hormonal levels was not found in intact animals, but by 2 months significant correlation appeared ( $R=0.87$ ), mainly on account of negative correlation with T ( $r_{xy}=-0.75$ ,  $P < 0.01$ ) and, to a lesser degree, with 17-CS ( $r_{xy}=+0.48$ ) and 11-HCS ( $r_{xy}=-0.37$ ).

In the male animal, reactivity of the lymphocytes to phytomitogens was thus physiologically dependent on hormonal factors. Bacterial prostatitis led initially to a complete disturbance of this dependence, evidently because of toxic influences from the pathological focus. The pathological dependence formed subsequently was due mainly to negative correlation between reactivity of the lymphocytes and androgens, by contrast with the original physiological positive correlation with corticosteroids. Considering previous observations showing direct correlation between T and lymphocyte reactivity during lowering of androgenic saturation of the body, the homeostatic character of the hormonal-lymphoid dependence relative to endogenous T must be assumed.

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