

# EFFECTS OF DISTURBANCE OF THE NORMAL COURSE OF PREGNANCY IN DOGS ON DEVELOPMENT OF NATURAL IMMUNITY IN THE PROGENY

V. I. Ermolov

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When the normal course of pregnancy in dogs was disturbed by stress, the immunologic properties of the blood of the fetuses and newborn puppies were appreciably weakened. The phagocytic response was depressed most sharply, and this was accompanied by a decrease in the digestive power of the leukocytes. Weakening of the immunobiological properties led to the appearance of inflammation in the lungs and intestine by the action of the automicroflora and was responsible for death of a large proportion of the newly born animals.

In a previous investigation the formation of natural immunity in the progeny of dogs with normal pregnancy was studied [3].

The purpose of the present investigation was to study changes in the development of physiological immunity in fetuses and puppies when the normal course of pregnancy in dogs is disturbed by stress. The antibody titer and the complementary, bactericidal, and phagocytic properties and the protein composition of the blood of the animals were investigated.

## EXPERIMENTAL METHOD

Shigella sonnei cells were used as the antigen. Antibodies were detected in the serum by the bulk agglutination method. Complementary activity was determined by a photolorimetric method in Gabrilovich and Soboleva's modification [2]. The bactericidal activity of the serum was determined after mixing of the serum and cultivation by counting the number of viable bacteria, and the result was expressed in Karolček's indices [5]. To study phagocytosis, the blood was mixed with 2.5% sodium citrate and a 2-billion suspension of bacterial cells in the ratio 2:1:1, incubated for 30 min at 37°C, and grown for 60 min on agar to reveal the digestive power of the neutrophils; the phagocytic index (PI), intensity of phagocytosis (IP), in per cent, and the degree of completion of phagocytosis (CP), in per cent, were calculated by the usual method. The normal course of pregnancy in the dogs was disturbed by I. A. Arshavskii's method. The stressors, which were applied from the 5th week of pregnancy, consisted of the loud noise of an automobile horn and an alternating current of 20 V, applied for 30 and 60 sec at intervals of 30 sec over a period of 1 h, repeated for between 3 and 9 times. As a control of metabolic changes taking place in the females, the following indices of acid-base balance of the urine were studied: pH, titratable acidity, titratable alkalinity, and ammonia by Conway's micromethod [4]. Fresh samples of urine collected before the beginning of stress stimulation and on the subsequent days of observation were tested.

## EXPERIMENTAL RESULTS

Disturbance of the normal development of pregnancy by exposure to stress was accompanied in most dogs by a marked shift of acid-base balance toward acidosis, by the development of albuminuria, and by a

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Rostov-on-Don Research Institute of Obstetrics and Pediatrics, Ministry of Health of the RSFSR.  
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TABLE 1. Dynamics of Immunologic Indices of Blood in Dogs (M ± m)

Age of animals	Number of tests	Titer of agglutinins	Titer of complement	Bactericidal index	Index of phagocytosis		
					PI	IP (in %)	CP (in %)
Fetuses, 9 weeks	12 (15)	1:5—1:10 (1:10—1:20)	33.8±3.0 (40.5±2.4)	0.10±0.06 (-0.01±0.08)	1.0±0 (1.2±0.05)	3.3±0.3 (6.3±0.07)	— (93.1±1.3)
Newborn puppies	55 (22)	1:10—1:20 (1:20—1:40)	50.2±1.9 (52.8±2.5)	0.41±0.06 (0.70±0.06)	1.4±0.1 (2.3±0.4)	1.9±0.4 (15.8±3.1)	75.2±1.9 (90.2±2.2)
4 days	55 (30)	1:20—1:40 (1:20—1:40)	104.9±1.6 (79.2±4.8)	1.42±0.07 (1.16±0.11)	1.9±0.1 (2.6±0.2)	15.2±1.8 (27.8±3.2)	72.0±2.2 (92.0±1.2)
8 days	32 (26)	1:20—1:80 (1:20—1:40)	108.5±6.7 (140.0±8.6)	1.11±0.10 (1.41±0.10)	1.5±0.1 (1.9±0.1)	5.6±1.3 (10.8±3.1)	77.7±1.9 (96.8±0.8)
12 days	27 (34)	1:20—1:80 (1:20—1:40)	112.3±6.5 (160.0±9.8)	1.35±0.13 (0.95±0.21)	1.8±0.3 (1.5±0.1)	4.6±1.4 (12.4±1.0)	81.2±2.6 (95.8±0.2)
21 days	32 (29)	1:20—1:80 (1:20—1:40)	128.5±5.7 (138.8±3.9)	1.28±0.14 (1.04±0.08)	2.1±0.2 (2.5±0.2)	7.9±1.4 (18.4±1.7)	82.1±1.9 (95.7±0.9)
28 days	32 (27)	1:40 (1:20—1:40)	118.9±6.4 (141.9±4.1)	1.15±0.09 (1.13±0.12)	1.5±0.09 (2.2±0.1)	6.6±1.0 (20.2±1.8)	73.9±3.0 (96.2±0.8)
Mothers	22 (19)	1:20—1:40 (1:40)	136.3±6.6 (111.8±5.4)	1.63±0.16 (1.57±0.15)	2.2±0.2 (3.6±0.3)	25.5±3.2 (44.2±2.9)	76.4±3.5 (95.5±1.1)

Note. Data obtained from normal animals given in parentheses.

worsening of the general condition. Eight of the 16 dogs went into labor prematurely (by 3–8 days). Regardless of the period of intrauterine development, most of the newly born puppies showed signs of physiological immaturity: small weight, low body temperature at birth (under 30–32°C), delay in acquiring vision, delay in standing, and weakening of the general resistance of the animals. This state of physiological immaturity in the fetuses and puppies was accompanied by a decrease in the total protein, albumins, and  $\gamma$ -globulins in the blood by comparison with normal animals. The appearance of maternal  $\gamma$ -globulins in the blood of the immature puppies was delayed because of delay in the secretion of colostrum by the females.

The results given in Table 1 show that at birth and during the first day of life the immunologic indices of the blood were appreciably depressed in these puppies. The phagocytic response of the blood was depressed most sharply, and this was accompanied by a decrease in the digestive power of the leukocytes.

Against this background of depressed immunobiological indices, many of the newly born puppies developed persistent inflammation, in the form of enteritis, catarrh of the respiratory tract, and suppurative conjunctivitis under the influence of the automicroflora (*Lactobacilli*, *Escherichia coli*, staphylococci). Of the total number of animals, 28.4 and 40.4% respectively died within the first 3–6 days. Histological examination of the organs from the animals revealed features of interstitial and parenchymatous pneumonia, with thickening of the interalveolar septa through infiltration by lymphocytes and histiocytes, with the presence of a few polymorphs, with the accumulation of exudate from lymphocytes and desquamated epithelial cells in the alveoli, with extensive areas of atelectases, and with circulatory disorders and bacterial emboli in the blood vessels. In the small intestine catarrhal inflammation of the mucous membrane with infiltration by lymphocytes together with necrosis of the epithelium of the villi were observed.

Starting on the 4th day, the indices of humoral immunity in the surviving puppies began to return to normal, but these changes were accompanied by hemoconcentration caused by the pathological state of the animals. The phagocytic activity of the leukocytes remained sharply depressed, and depression of function of the cells was accompanied by a decrease in their glycogen content.

Disturbance of the normal course of pregnancy by exposure to stress thus weakens the development of natural immunity and depresses the resistance of the newly born animals. These disorders evidently arise through changes in the functional state of the hypothalamo-hypophyseal-adrenal and sympathico-adrenal systems under the influence of stress, accompanied by inhibition of the mechanism of neuro-hormonal regulation of pregnancy and disturbance of the conditions ensuring normal development of fetuses and newborn animals [1].

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