

CAPILLARY CIRCULATION IN EXPERIMENTAL PLAGUE

K. M. Mokhin

From the State Institute of Scientific Research Against Plague of the Ministry
of Public Health USSR (Director — A. K. Shishkin) Rostov-on-Don

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Circulatory disturbance is one of the basic symptoms of the plague. However, the mechanism of circulatory insufficiency in this infection remains almost uninvestigated. Morphologic investigations in plague point to a considerable involvement of blood vessels, especially capillaries [1, 3-5]. Physiological verification of the physiological state of the various divisions of the vascular system in plague remains undone.

Taking into consideration the important role of capillary blood flow in the general circulatory system, we decided to investigate the character of the capillary blood circulation at various stages of experimental plague infection. Changes in the intensity of tissue circulation were evaluated by the alteration in the resorption of substances of low molecular weight from the site of infection. The latter was determined with the method of labeled atoms.

It is known that compounds of low molecular weight are removed from the site of injection mainly by the system of blood capillaries, whereas compounds of high molecular weight — principally by the system of lymphatic capillaries [2, 6, 7, 9]. Therefore the rate with which a radioactive isotope combined with a compound of low molecular weight is removed from tissue can serve, to a certain degree, as an index of the status of capillary blood circulation. Under these conditions the absorption time depends on the intensity of blood circulation, the number of functioning capillaries and the state of capillary permeability [8, 10].

EXPERIMENTAL METHOD

Experiments were carried out on guinea pigs. A hypodermic injection of 0.1 ml solution of $\text{Na}_2\text{HP}^{32}\text{O}_4$ was given with a tuberculin syringe into the previously hair-clipped area of the abdominal wall. The concentration of P^{32} was chosen so that the number of impulses at the beginning of the recording would be within the limits of 1,000 per minute. Impulses were recorded with apparatus B equipped with counter AC-2, which is enclosed in a lead membrane with an aperture 12 mm in diameter. The counter was situated above the site of injection of the radioactive substance and 1 cm from it. The intensity of irradiation was recorded at one minute intervals throughout the experiment.

Half-absorption time or the time necessary for absorption of half of the quantity of isotope introduced was used as an index of the rate of resorption. The process of resorption was depicted graphically in a system of semilogarithmic coordinates: the abscissa axis — time in minutes, the ordinate axis — logarithm of the number of impulses. The half-absorption time was calculated from the graph. The data obtained was processed statistically.

The intensity of the resorption of the isotope introduced was determined 3-4 times on healthy guinea pigs. The animals were then infected by the subcutaneous injection of a virulent strain of *B. pestis* 773. The infected dose consisted of 1000 microbes which is equal to 100 Mld. This was followed by daily determinations of the status of capillary blood flow in the dynamics of the plague infection.

Simultaneously, an investigation of the pathologico-anatomical and bacteriological picture of the

Infectious process was carried out by daily autopsies of 1-2 pigs following the determination of the rate of resorption of the isotope introduced. This clarified the character and degree of pathologico-anatomical changes and at the same time agar media were inoculated with subcutaneous tissue from the site of the infected regional lymph node, and from the spleen, liver, lungs and blood.

EXPERIMENTAL RESULTS

In experimental plague infection retardation of the resorption rate of $\text{Na}_2\text{HP}^{32}\text{O}_4$ was observed. Table 1 shows that within 24 hours after infection the half-absorption time was prolonged in all guinea pigs receiving the isotope. If prior to the infection the average half-absorption time was 12.1 minutes, 24 hours after infection it was found to be 20.3 minutes. Statistically this difference is entirely reliable ($P < 0.001$).

TABLE 1

Study of the Rate of Resorption of $\text{Na}_2\text{HP}^{32}\text{O}_4$ Introduced Subcutaneously in the Process of Developing of Experimental Plague Infection

Guinea pig number	Half-removal time of isotope at various periods following infection							Number of days between infection and sacrifice or spontaneous death
	prior to infection	period following infection (in days)						
		1	2	3	4	5	6	
1	10	21	—	—	—	—	—	1 (s)
2	13	20	27	—	—	—	—	2 (s)
3	10,5	29,5	55	54	—	—	—	3 (s)
4	12,5	18	25	29	—	—	—	3 (s)
5	11,5	19	31	36	43	—	—	4 (s)
6	9,5	18,5	43	54	—	—	—	3
7	10,5	19	23	32	52	—	—	4 (s)
8	12	21,5	29	37	49	67	—	5
9	11,5	22,5	27	43	58	—	—	4
10	14,5	19	34	58	—	—	—	3
11	12	16,5	19	29	32	38	—	5
12	9,5	14,5	24	37	43	65	—	5
13	12	23	37	44	55	—	—	4
14	15	16	31	51	62	—	—	4
15	16	23	28	39	44	70	—	5
16	13,5	20,5	28	34	49	61	—	5 (s)
17	9,5	19	31	36	41	—	—	4
18	14,5	16	29	40	44	49	60	6 (s)
19	10,5	27	37	55	—	—	—	3
20	14	24	31	43	67	68	—	5
M	12,1	20,3	29,4	44	49,1	59,7	60,0	—

Prearranged designations: M — arithmetical mean values; y) sacrificed.

During this period of the infectious process pathologico-anatomical changes were not observed and a culture of B. pestis was isolated only from the site of injection (Table 2).

Two days after infection resorption time exceeded the initial by more than twice. Plague microbes were found at the site of injection and in the regional axillary lymph nodes. The pathologico-anatomical picture is limited by a slight edema of the subcutaneous tissue and by punctate hemorrhages in the regional nodes.

The first changes in the viscera in the form of enlargement of lymph nodes, and hyperemia of the liver and spleen were observed on the 3rd — 4th day. Four days after infection plague microbes were found in all organs examined. Isotope resorption time at this stage of the disease exceeded the initial by more than 4 times. As the infectious process progressed, the resorption time progressively increased and on the 5th day of the disease reached the mean of 59.7 minutes, i.e. almost 5 times greater than the initial time.

Especially abrupt was the decrease of the absorption of isotope in terminal guinea pigs (half-removal isotope time — 65 — 70 minutes). Taking into consideration the fact that the rate of resorption of substances of low molecular weight reflects the intensity of tissue circulation, one may assume that in experimental plague infection there is an abrupt lowering of the intensity of peripheral blood circulation.

TABLE 2

Rate of Resorption of Isotope, Infectiousness of Organs and Pathologico-anatomical Changes in the Dynamics of Plague Infection

Animal number	Days between infection and sacrifice of animal	Half-removal time in minutes		Inoculation of <i>B. pestis</i> from organs						Localization of pathologico-anatomical changes
		prior to infection	on the day of autopsy	site of infection	lymph node	spleen	liver	lung	blood	
1	1	10	21	+	—	—	—	—	—	Not indicated
2	2	13	27	+	+	—	—	—	—	LN
3	3	10,5	54	+	+	+	+	+	+	LN, S
4	3	12,5	29	+	+	+	+	—	—	LN, L
5	4	11,5	43	+	+	+	+	+	—	LN, S, L
7	4	10,5	52	+	+	+	+	+	+	LN, S, L
16	5	13,5	61	+	+	+	+	+	+	LN, S, L, LS
18	6	14,5	60	+	+	+	+	+	+	LN, S, L, LS

Prearranged designations: — *B. pestis* culture isolated; — *B. pestis* culture not isolated; LN) lymph node; S) spleen; L) liver; LS) lung.

Comparison between the intensity of absorption of isotopes and the dynamics of infectiousness of organs and their pathologico-anatomical changes at various stages in the course of experimental plague infection showed that disturbances of absorption and, therefore, of capillary blood circulation appear considerably earlier than the visible pathologico-anatomical changes and precede the distribution of plague microbes from the site of injection into the blood and viscera.

SUMMARY

Capillary circulation was examined in experimental plague of guinea pigs. The rate of removal of radioactive phosphorus beyond the limits of the site of injection served as an indicator of the intensity of capillary circulation in healthy and infected animals.

During plague the rate of resorption of radioactive phosphorus is considerably diminished, which points to the decreased intensity of capillary circulation. Disturbances of circulation occur before the appearance of any visible pathologico-anatomical changes and precede the entrance of plague bacilli into the internal organs and blood.

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