THE RATE OF BLOOD FLOW IN EXPERIMENTAL BUBONIC PLAGUE

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Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 53, No. 2, pp. 47-52, February, 1962
Original article submitted February 17, 1961

Clinical observations indicate that in bubonic plague there occur major disturbances in the blood circulation [3-5]. However, the character and severity of these disturbances has been studied most inadequately. Such hemodynamic indices as the rate of blood flow, circulating blood volume, and systolic and minute volume of the heart have not yet been the subjects of investigation in clinical dealings with plague or in experimental plague infection.

In studying the characteristics of the hemodynamic disturbances associated with experimental bubonic plague, we decided to determine the rate of blood flow and the circulating blood volume in addition to investigating the electrocardiogram [1] and the capillary circulation [2].

This report presents data from studying the rate of blood flow in experimental bubonic plague, using guinea pigs and rabbits.

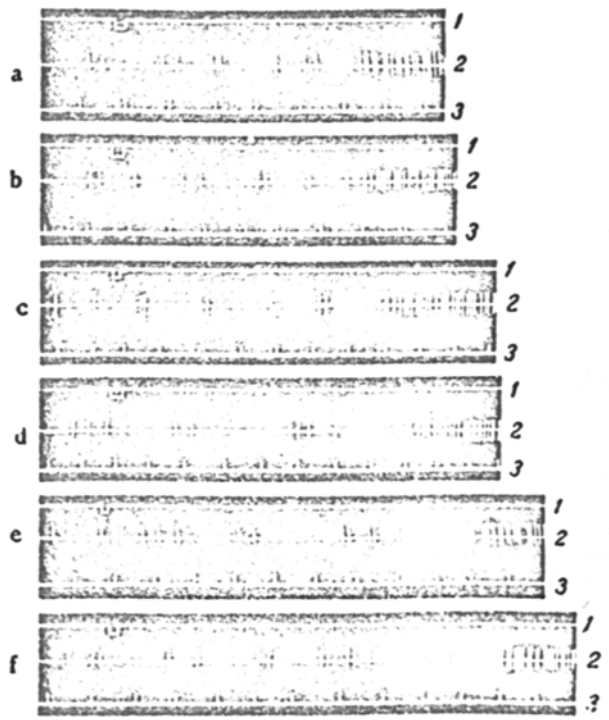
TABLE 1. Rate of Blood Flow (in seconds) in Guinea Pigs as Affected by the Dynamics of Plague Infection

Guinea pig No.	Before inoculation	At different intervals following inoculation (in days)						Guinea pig No.	Before inoculation	At different intervals following inoculation (in days)						
		1	2	3	4	5	6			1	2	3	4	5	6	7
1	5½	5½	6	7	8½	9	—	18	5	5	4½	5	7	8½	9	—
2	5	5	5	6½	8	9½	—	19	5½	5½	6	6½	7	8	—	—
3	6	6	5½	6	6½	8	10½	20	5	5	4½	5	6	8	10	11
4	5	5½	5½	7	8½	9½	—	21	5	5	5½	6	8	8½	—	—
5	5	5½	6	6½	8	—	—	22	6	6	5½	6	7	8½	11	—
6	4	4½	6	7½	9	10	—	23	5	5	6	6	6½	9	—	—
7	6	6	6½	7	10	11	—	24	5½	5½	5	6	8	9	10	—
8	5½	5½	6½	7½	9	10	—	25	6	6	5½	7	9	10	—	—
9	4½	4	4½	5	7	9½	—	26	5	5	4½	6	7½	9	10	—
10	5	5½	6½	7	7½	—	—	27	5	5½	6½	6½	7½	—	—	—
11	5	6	6½	7½	9	10	—	28	5	5½	6	7½	8	9½	—	—
12	5½	5½	5½	6	7	9½	—	29	5	5	6½	7	7½	9	—	—
13	6	6	5½	6½	8	9	—	30	6	6½	6½	7	7½	9	9½	—
14	5	6½	5½	7	9½	—	—	31	5½	5½	6½	6½	7	7½	—	—
15	5	5	5½	7	10	—	—	32	5	5	5	6	7½	8	10	—
16	5	5	4½	5	6½	9	10	33	5½	5½	5	5½	6	7	9	9½
17	6	5½	5½	6	7½	9½	11	34	5	5½	6	6½	8	9	—	-

EXPERIMENTAL METHOD

The experiments were set up on 34 guinea pigs and 18 rabbits. The rate of blood flow was determined by the radiometric method. For this, radioactive indicators – a solution of $Na_2HP^{32}O_4$ or $Na^{24}Cl$ – were injected into the marginal ear vein of the rabbit, or in the guinea pig, into a superficial vein of the hind paw via a small skin incision. The rate of blood flow in the guinea pigs was evaluated from the time necessary for the passage of the radioactive

isotope from the site of injection to the other posterior extremity; for the rabbits – passage to the other ear. To record the impulses, we used the apparatus B, with the AS-2 counter, which was enclosed in a lead casing with a small aperture, and attached to the surface of the guinea pig's leg or the rabbit's ear. For a graphic recording of the impulses, we used a marker which we constructed, making it possible to determine objectively the moment of the radioisotope's appearance. The moment of injection of the radioisotope, the intensity of the impulsation, and the time in seconds, were recorded on a kymograph drum.



Change in the rate of blood flow within the dynamics of a developing plague infection (guinea pig No. 11). a) Prior to inoculation; b, c, d, e, f) 1st, 2nd, 3rd, 4th, and 5th days after the inoculation; 1) marking of the isotope injection; 2) recording of the impulses; 3) time markings (1 second).

The rate of blood flow in the experimental animals was determined prior to inoculation, and following inoculation of subjects with a virulent strain of B. pestis No. 773, daily, in dynamic relation to the plague infection. The guinea pigs were inoculated subcutaneously in the left anterior extremity. The inoculating dose was 1000 microbial bodies, which corresponded to 100 Dlm. Out of 18 rabbits, 12 were inoculated subcutaneously in the anterior extremity; the inoculating dose was 5-6 billion microbial bodies. The remaining 6 rabbits were inoculated intravenously; the inoculating dose was 3 billion microbial bodies.

In addition to studying the rate of blood flow, we investigated the pathologico – anatomical and bacteriological picture of the infectious process. Seeding to agar media was performed from a regional lymph node, the spleen, liver, lungs, and blood.

EXPERIMENTAL RESULTS

In the first series of experiments, determining the rate of blood flow in the guinea pigs, it was established that prior to inoculation it was equal to 5-6 seconds in the majority of the animals (in 31 out of 34). The rate of blood flow was a little greater in only 2 of the guinea pigs and for passage of the radioactive isotope from the blood stream of the left posterior to the right posterior extremity required 4-4½ seconds. Repeat determinations demonstrated the rate of blood flow to be relatively constant for each healthy guinea pig.

Following inoculation of the guinea pigs with the virulent plague strain, the rate of blood flow changed in correspondence with the dynamics of the plague infection. In the first period (1st-2nd day), the characteristics of the change in blood flow rate were not uniform in all the experimental guinea pigs. While a decrease in the rate of blood flow by ½-1½ seconds was already noted in the first period of the plague infection in 19 of the guinea pigs, in 11 of the guinea pigs the rate of blood flow at that time showed a tendency towards increasing, and the time needed for the radioactive isotope to make the circuit was shorter by ½-1 second. In the remaining 4 guinea pigs, the rate of blood flow did not change within the first 2 days following the inoculation (Table 1).

A comparison of the nature of the change in the rate of blood flow with the character of the course of the plague process showed that, as a rule, in the cases where the plague infection progressed rapidly, with death of the guinea pigs on the 4-5th day, the rate of blood flow decreased as early as the 1-2nd day following the inoculation. If the infectious process extended into the 6-7th day, then there was usually some increase in the rate of blood flow during the first period.

Further, beginning with the 3rd-4th days after the inoculation, we observed a gradual decrease in the rate of blood flow of all the guinea pigs used in the experiment.

On the day of the animals' death, the rate of blood flow was not similar in all the animals. In 5 of the guinea pigs it decreased minimally up until that time, and was equal to 7½-8 seconds. In the remaining 29 animals, the rate of blood flow on the last day was 10-11 seconds, i.e. was half that of the original rate, observed prior to inoculation.

TABLE 2. The Rate of Blood Flow (in seconds) in Rabbits Within the Dynamics of a Plague Infection

Means of inoculation	Inoculating dose (in billions of microbial bodies)	Before inoculation	At different intervals following the inoculation (in days)												The number of days after the inoculation that the rabbit either died or was sacrificed
			1	2	3	4	5	6	7	8	9	10	11	12	
Intravenously	3	6	6	7	8	8½	11	—	—	—	—	—	—	—	5
	3	5½	5½	5½	—	—	—	—	—	—	—	—	—	—	2
	3	6	6	6	—	—	—	—	—	—	—	—	—	—	2
	3	5	5½	6	7½	8	9	11½	—	—	—	—	—	—	6
	3	5½	6½	7	8	9	10	10½	10½	11	—	—	—	—	8
	3	5½	6	7½	7½	9½	10	10	—	—	—	—	—	—	6
Subcutaneously	5	5½	6	7	7½	8½	8	8½	9	9	10	—	—	—	9
	5	6	6½	7	9½	9½	10	—	—	—	—	—	—	—	5
	5	6	6	5½	6	6½	7	7½	7	7½	6½	6½	6	6	20(s)
	5	5½	6	7	7	8	8½	9	—	—	—	—	—	—	6
	6	6½	7	7½	9	10½	10	11	11	—	—	—	—	—	7
	6	5½	5½	7½	8½	8½	9	9½	10	—	—	—	—	—	7
	6	6½	6	6½	6½	7	7	8	7½	8½	8	7½	7½	7	27(s)
	6	6	6	5½	5½	6	7	7½	7	7	6½	6½	6½	6	18(s)
	6	5½	5½	7½	8	9½	9½	—	—	—	—	—	—	—	5
	6	6	6½	8	8	8½	9	10	10	—	—	—	—	—	7
	6	6	5½	5	6	6	6½	7	7	7½	7½	6½	6	5½	27(s)
	6	5½	6	7½	8	9	9	10	10½	—	—	—	—	—	7

Symbols: s — sacrificed.

For example, in guinea pig No. 11 the rate of blood flow before the inoculation was equal to 5 seconds; after 24 hours, a slowing of the rate by 1 second was noted. With further development of the plague process, there was a gradual slowing of the rate of blood flow, and by the 5th day after the inoculation, the day of the animal's death, the rate of blood flow was equal to 10 seconds (see figure).

On autopsy, the typical pathomorphological picture for bubonic plague was observed in all the guinea pigs that died. Seeding from the organs produced growth of the plague bacillus.

In the second series of experiments, we studied the rate of blood flow in rabbits with experimental bubonic plague.

Rabbits are less susceptible to B. pestis than guinea pigs. Therefore, in order to obtain a clearly defined plague process, leading to the death of the experimental animals, we increased the inoculating dose markedly. The infectious process in the rabbits occurred especially intensely with intravenous injection of the B. pestis. However, with the huge inoculating doses, injected intravenously, the rabbits died after 1-2 days without apparent pathomorphological changes characteristic for the plague infection.

In our experiments with intravenous inoculation of the rabbits, 2 animals died after 2 days. The rate of blood flow in this case did not change (Table 2). It must be noted that these animals did not manifest clear cut signs of the illness, and only 1-1½ days prior to their deaths were there noted such signs as general sluggishness, adynamia, and rapid breathing. On autopsy, we did not observe any apparent pathomorphological changes. A culture of B. pestis was not isolated. In the remaining 4 rabbits, inoculated intravenously and dying on the 5th-8th days, an appreciable lowering of the blood flow rate was noted. While it was equal to 5½-6 seconds prior to the inoculation, it slowed to 10-11½ seconds by the day the animals died. On autopsy, we observed the characteristic pathomorphological picture. A culture of B. pestis was isolated from all seedings of the organs.

Of the 12 rabbits that were inoculated subcutaneously, 8 died on the 5-9th day after inoculation. In these rabbits, we observed slight slowing of the rate of blood flow during the first period, which became more and more pronounced as the plague process developed. As can be seen from Table 2, the rate of blood flow in the last days was 1½-2 times lower than the original. On autopsy, we observed the typical pathomorphological picture of bubonic plague. Upon seeding the material from the organs, the plague microbe was isolated in all cases.

The remaining 4 rabbits, inoculated subcutaneously with the same dose, were sacrificed on the 18-27th days after the injection. In these rabbits, we noted a slight increase in the rate of blood flow in the first 2-3 days, following which it slowed by 1-1½ seconds. By the 11-12th day, as the state of the animals improved, the rate of blood flow increased to the original level, observed prior to inoculation. In these cases, autopsy of the rabbits did not disclose the pathomorphological changes typical for bubonic plague, and the plague microbe was not isolated.

On the basis of the data obtained, it appears that in guinea pigs suffering from plague, with the characteristic pathomorphological changes and seeding of the plague microbes from the organs, the rate of blood flow is slowed by almost half in comparison with the original level. In the cases where the plague infection progressed rapidly, a decrease in the rate of blood flow was observed even on the 1st day after inoculation of the animals, which gradually progressed with development of the disease process.

Where the plague infection progressed more slowly, a certain increase in the rate of blood flow occurred in the first period, subsequently changing to a slowing. If inoculation of the animal failed to cause its death, then as its condition improved the rate of blood flow normalized.

Changes in the rate of blood flow, reflecting the seriousness of the plague process, appear to be an important index, characterizing a hemodynamic disturbance associated with this infection.

SUMMARY

The circulation rate was studied during experimental plague in guinea pigs and rabbits by means of the isotope method. In guinea pigs with a rapid course of plague infection, with the animals' death occurring on the 4th-5th day, the circulation rate decreases 1-2 days after the infection. With a more torpid infectious process the circulation rate showed some rise during the initial period. Beginning from the 3rd-4th day after the infection in all the guinea pigs there was seen a 1½-2 reduction of the circulation rate in comparison with the initial one. In rabbits suffering from typical plague with characteristic pathologico-anatomical changes and bacteriological isolation of Bacillus pestis from the organs, the circulation rate during the infectious process is almost halved in comparison with its initial value.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
