HEREDITARY TRANSMISSION OF PLAGUE RESISTANCE IN PALLASIOMYS MERIDIANUS

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[Following is the translation of an article by M. I. Levi, et. al. in the Russian-language journal Byulleten' Eksperimental'noy Biologii i Meditsini (Bulletin of Experimental Biology and Medicine), No 7, 1963, pages 75-79.]

From the Rostov-na-Donu Scientific Research Antiplague Institute and the Astrakhan' Anti-Plague Station

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In comparative experiments it has been possible to establish essential differences in the extent of resistance to plague in noon jerboas inhabitating the left and right banks of the Volga, and also related differences in the pathogenesis of the infection, ~~(2-5)~~. When the subcutaneous method of infection is used the LB_{50} for left-bank noon jerboas exceeded the LB_{50} for right-bank jerboas by several dozens of thousands or hundreds of thousands of times. The geographical isolation of the right-bank and left-bank noon jerboas is not subject to doubt.

In this report we ~~studied~~ the effect, ~~the~~ genetic factors on formation of plague resistance in left-bank noon day jerboas.

Experimental Methods

Initially the conditions of propagation of noon jerboas in captivity were elucidated (4). The animals multiplied well in concrete poultry yards. A special diet was required for the feeding of the animals. Under strictly controlled conditions cross breeding of noon jerboas in two lines was carried out. In the first line left-bank females and right-bank males were crossed, and in the second line -- left-bank males and right-bank males. The hybridization succeeded, and the progeny obtained proved fertile. During the first and second generations of the progeny of each line males and females were paired.

The work continued from mid 1960 to 1962.

In all three experiments were performed on infection Pallasiomys meridianus with a virulent strain of plague bacillus (strain No. 1230 of the jerboas variety), similar to the strain studied previously (8). In the first experiment the parental generation of the jerboas underwent infection, in the second -- the progeny of the first generation, and in the third -- the progeny of the second generation. In addition to infection of the progenies of both lines the same doses were administered simultaneously to right-bank and left-bank Pallasiomys meridianus trapped in the Steppe, to left-bank Pallasiomys meridianus raised in captivity, and to white mice. Inoculation of infecting doses in nutrient agar was carried out in parallel. The doses for infection were as follows: 0.1, 1, 10, 100, 1000, 10,000, 100,000, 1,000,000, 10,000,000, 100,000,000 bacterial bodies, each dose was given subcutaneously to males and females of each group of animals of approximately the same weight (the same dose to each of eight animals).

As the animals perished, they were dissected, inoculations in nutrient agar were made and in broth material taken from the site of injection, regional lymph nodes, spleen, liver, lungs, and blood. For half of the animals, from the moment of infection and up till the tenth day, the quantitative content of plague bacillus in the peripheral blood from the incision of the tail was studied each eight hours by way of its inoculation on solid nutrient medium. All the surviving animals were sacrificed 21 days after infection for bacteriological examination, and the sera was investigated in the hemagglutination-inhibition reaction formalinized sheep erythrocytes sensitized with fraction 1 to detect antibodies to the plague bacillus. The details of method of the experiment are given an article by M. I. Levi (6).

In addition to the experiments on determination of resistance to plague in progeny of Pallasiomys meridianus biometric measurements of the animal body and skull were made.

Experimental Results

The results of all the experiments on infection of the progeny of Pallasiomys meridianus of both lines proved monotypical (Table 1). If the dose responsible for the death of 50 animals, was dozens or hundreds of bacilli for white mice, for left-bank Pallasionys meridianus it was less than 10, in the 10's or hundreds of bacilli, for left-bank

Pallasiomys meridianus (both for animals trapped in the Steppe as well as for those raised in the laboratory), the dose was in the several and tens of millions, while for the progeny of both lines in two generations this dose value ranged within the limits of several, tens and hundreds of thousands of bacterial bodies. Thus, the LD_{50} in the progeny was approximately the mean value between the LD_{50} for right-bank Pallasiomys meridianus and the LD_{50} for left-bank. Calculations of the LD_{50} shown in Table 1 are compared with observations of animals for which the tail incisions of bacterial study were not made.

TABLE 1

Resistance of Progeny Obtained as a Result of Crossing Right-Bank and Left-Bank Pallasiomys meridianus (LD_{50} in bacterial bodies)

(a) Характеристика животных	(b) № опыта 1	2	3
(c) Белые мыши	316	558	48
(d) Правобережные полуденные песчанки	4	216	2
(e) Левобережные полуденные песчанки	3 937 000	>10 000 000	39 400 000
(f) Первое поколение первой линии		1 000	14 920
(g) Второе поколение первой линии			170 000
(h) Первое поколение второй линии		131 000	
(i) Второе поколение второй линии			56 200

LEGEND: a) characteristics of the animals; b) number of experiments; c) white mice; d) right-bank Pallasiomys meridianus; e) left-bank Pallasiomys meridianus; f) first generation of first line; g) second generation of first line; h) first generation of second line; i) second generation of second line.

As an example we present results of a study of bacteriemia in one group of animals (Figure 1). In accordance with the previously established regularity bacteriemia in right-bank Pallasiomys meridianus developed after infection with minimal doses, and was agonal in character; enormous amounts of bacteria were found in the blood. Bacteriemia in left-bank jerboas developed from large doses; in addition to the

agonal bacteriemia, the infectional variety was found, when there were only several bacteria per mm^3 of blood. In the progeny of jerboas of both lines bacteriemia was found to have properties characteristic of the bacteriemia of both right-bank and left-bank jerboas (Figures 2 and 3). The indices of bacteriemia which were calculated in accordance with a method recommended by M. I. Levi (5) are mean indices for each group of animals.

Antibodies to plague bacillus appeared infrequently and in low titer in the serum of right-bank jerboas surviving after infection, while they were found in several cases in left-bank jerboas and in the progeny of both lines, in titers from 1:40 to 1:5120. We also noted that the highest antibody titers were recorded not so much for jerboas for which bacteria had been detected in the blood (however, they survived) as much as for animals for whom an abscess containing live bacteria had formed at the injection site 3 weeks after infection.

Biometric measurements allowed us to establish that features characteristic of the progeny of both lines can serve as intermediate for left-bank and right-bank Pallasiomys meridianus (Table 2).

Based on the fact that differences in resistance in right-bank and left-bank Pallasiomys meridianus have been established only with respect to plague causative, but not to other pathogenic microorganisms, and also based on the leading role which left-bank Pallasiomys meridianus play in sustaining the existence of the plague bacillus in nature (right-bank jerboas have no essential significance to the existence of natural focus), the suggestion was made (5) that the resistance of left-bank jerboas to plague is a consequence of the centuries old involvement of these animals in the epizootic progress. A similar point of view has been held by Ye. S. Biryukova (1). L. A. Zil'ber does not deny such a possibility, when he states that in this way natural species immunity (3) can thus arise. At the same time Yu. M. Yelkin appraised this suggestion as invalid. He noted that similar facts have been found in studying resistance to plague in Persian /persidskiye/ jerboas. Baltazar (1953) found that Persian jerboas in having the rocky locality of Iranian Kurdistan, where they play a leading role in sustaining the natural focus of plague, are very resistant to experimental infection with plague. However, U. A. Mamed-zade, working with the Persian jerboas living within the limits of Azerbaydzhanskaya SSR, only 100 km to the north, where these animals are of no significance in sustaining the existence of the plague bacillus, has shown that they do not exhibit resistance to plague (7).

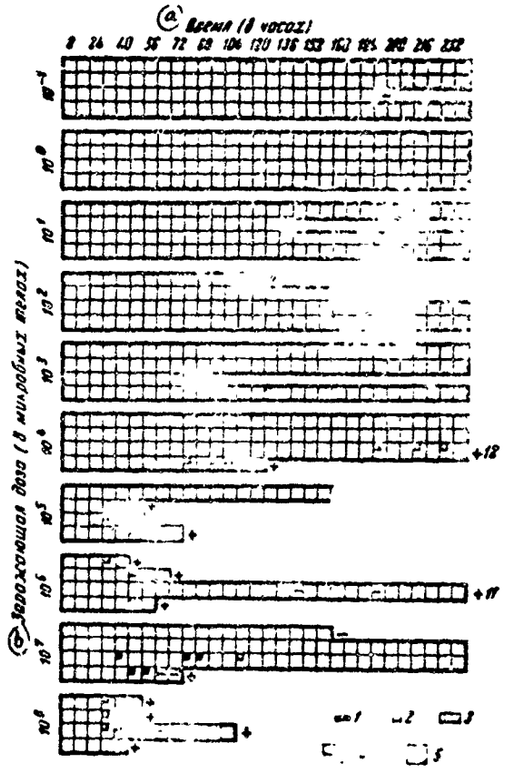

Figure 1. Bacteremia in animals of the second generation of the first line (F_1 - 1). Experiment No 3. + = plague bacteria isolated from succumbed rodent; + 12 = day on which the rodents succumbed; 1 - plague bacteria not isolated; 2 - from one to twelve colonies isolated; 3 - from 11 to 50 colonies; 4 - from 51 to 100 colonies; 5 - more than 100 colonies.

LEGEND: a) time (in hours); b) infecting dose (in bacterial bodies).

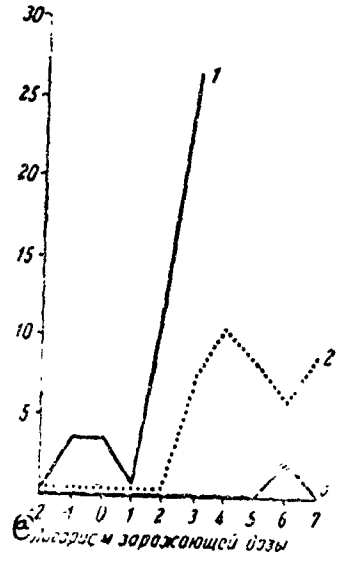

Figure 2. Curve of bacteriemia indices. Experiment No 2. 1 - right-bank Pallasiomys meridianus; 2 - $F_2$2 generation; 3 - left-bank Pallasiomys meridianus.

LEGEND: a) logarithm of infecting dose.

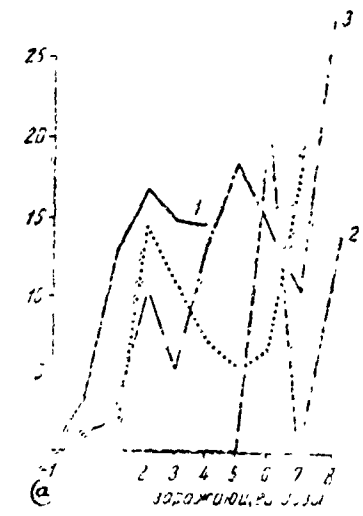

Figure 3. Curve of bacteriemia indices. Experiment No. 3. 1 - right-bank Pallasicmys meridianus; 2 - left-bank Pallasiomys meridianus; 3 - generation F_2-1; 4 - generation $F_2$2.

LEGEND: a) logarithm of infecting dose.

TABLE 2

Comparative morphology of the characteristics of two populations of Pallasiomys meridianus and their progeny (age of animals -- 7-10 months)

a	b	c	d	e	f	g	h
				в мм			
i) Левобережные песчанки, выловленные в природе	20	39	97	27	14	[illegible]
	51	41	95	27	14	[illegible]
j) То же	[illegible]	[illegible]	92	27	13	[illegible]
	10	38	93	27	13	[illegible]
k) Левобережные песчанки, выращенные в питомнике	8	30	91	26	14	[illegible]
	11	38	93	26	14	207
l) Правобережные песчанки, выловленные в природе	35	40	102	27	14	[illegible]
	65	44	102	28	15	[illegible]
m) То же	26	41	98	27	14	214
	23	51	97	27	14	224
n) Первое поколение первой линии	20	45	94	26	13	214
	18	55	93	26	14	[illegible]
o) Первое поколение второй линии	10	35	92	27	14	202
	30	41	93	28	15	210
p) Второе поколение второй линии	28	40	95	27	14	211
	30	49	94	28	14	216

Remark: First number = females, second = male.

LEGEND: a) group of jerboas; b) number of specimens undergoing measurement; c) average indices; d) weight (in grams); e) length of tail without end hairs; f) length of front paw not counting claws; g) height of ear; h) overall length from end of snout to end of tail, without fur; i) left-bank jerboas trapped in nature; j) as above; k) left-bank jerboas raised in refuge; l) right-bank jerboas trapped in nature; m) as above; n) First generation of first line; o) First generation of second line; p) Second generation of second line.

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