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CROSS-IMMUNE REACTIONS BETWEEN PANAMANIAN STRAINS OF Q FEVER AND ENDEMIC TYPHUS

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In 1939 Dyer (1) reported the results of his experiments on cross-immunity between the Australian "Q" and American "X" strains of *Rickettsia burneti* and the "W" strain of endemic typhus. He found no cross-immunity between the American Q fever and the typhus strains, but did find a partial immunity produced by the typhus against the Australian Q fever strain.

In 1947 we (2) isolated an interesting strain of *Rickettsia burneti* from the blood of a patient with Q fever in Panama, which shares some of the characteristics of both the Australian and American varieties. It seemed of interest, therefore, to determine whether there might be cross-immunity between this strain and a local strain of murine typhus.

DESCRIPTION OF STRAINS

Rickettsia burneti (strain JD). A detailed description of this strain has been published elsewhere (2). However, we may briefly summarize those characteristics most pertinent to this study. It was isolated in March of 1947 from the blood of a 33-year-old Panamanian salesman (J. D.), with clinically typical Q fever, and has been maintained since that time by continuous passage in guinea-pigs and embryonated hen's eggs. Guinea-pigs inoculated with homologous blood or tissues develop a high sustained fever of 2 to 6 days duration after an incubation period of 3 to 12 days. There is no local or testicular reaction. Mortality averages 30 per cent and usually occurs after a period of apparent recuperation. Guinea-pigs inoculated with yolk sac suspensions show a shortened incubation period and a more severe infection with an invariably fatal outcome. This strain gives complete reciprocal cross-immunity with an Italian strain (received through the courtesy of Dr. R. J. Huebner). One attack confers an immunity lasting at least 8 months.

Rickettsia prowazeki var. mooseri (strain SM). This strain was isolated in April 1947 from the blood of a 40-year-old Panamanian baker, S. M., with a mild but typical typhus fever with a well-developed eruption and a positive Weil-Felix reaction in titer of 1–320. It produces a relatively low grade, at times intermittent febrile reaction in approximately 80 per cent of guinea-pigs inoculated with homologous tissue suspensions or blood. About 70 per cent of well-developed male pigs show a moderate to severe testicular reaction. There is no spontaneous mortality except after injection with yolk sac suspensions when from 25 to 50 per cent die.

METHODS

All inoculations were made by the intraperitoneal route. Guinea-pigs immunized to one strain were tested in 17 to 43 days against the other. Tempera-

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tures were taken once daily at approximately the same hour of the morning prior to feeding. In normal animals temperatures similarly taken very rarely exceed 102.6°F. However, we have used 103.0°F. as the lower limit of a febrile reaction. Blood used as the infecting inoculum was taken by cardiac puncture on

TABLE I

Reactions in guinea-pigs inoculated with murine typhus after previous immunization to Q fever

NO. OF EXPERIMENT	ANIMAL NO.	NO. DAYS BETWEEN INOCULATIONS	INFECTIVE INOCULUM	INCUBATION PERIOD	DURATION OF FEVER	MAXIMUM TEMPERATURE	TESTICULAR REACTION*
					days		
I	1†	25	Emulsion spleen and liver	10	1	103.2	M
	2†	25		—	—	101.4	0
	3	25		—	—	102.2	0
	4	control		8	1	103.4	S
	5	control		6	3	103.5	S
	6	control		6	1	103.4	M
II	7	18	Blood	9	2	103.8	0
	8	18		—	—	102.8	0
	9	control		—	—	102.4	0
	10	control		8	1	103.0	M
III	11	43	Emulsion brain	9	4	104.2	0
	12	43		—	—	102.7	0
	13	43		—	—	102.6	0
	14	control		9	4	104.4	M
	15	control		11	2	103.5	S
	16	control		—	—	102.3	0
IV	17	42	Testicular washings	—	—	102.8	0
	18	42		6	4	103.8	M
	19	control		—	—	102.3	M
	20	control		2	2	103.6	M
V	21	31	Yolk sac suspension	9	5	103.5	0
	22	37		7	2	103.0	0
	23†	control		7	6	104.0	M
	24	control		7	3	103.4	0

* M indicates a moderate reaction with erythema, edema and difficult retractability. S indicates a severe reaction with firm adhesions and ecchymoses.

† Guinea-pig No. 1 died in 13 days, No. 2 in 7 days and No. 23 in 11 days after inoc.

the second or third day of fever. Tissue extracts similarly were prepared from animals sacrificed during the febrile period.

RESULTS

Detailed results are presented in Tables I and II. These may be summarized briefly as follows. Guinea-pigs infected with murine typhus fever 18 to 43 days after inoculation with Q fever showed somewhat variable results which may be

attributed in part to the relatively low pathogenicity of the SM strain and in part to the effects of the late residual activity of the JD strain of *R. burneti*. Only 6 of 12 Q fever immune pigs gave a definite febrile reaction whereas 9 of 12 controls showed febrile temperatures. The average length of the febrile reaction and the average incubation period, however, were without significant difference

TABLE II

Reactions in guinea-pigs inoculated with Q fever after previous immunization to murine typhus

EXPERIMENT NO.	ANIMAL NO.	NO. DAYS BETWEEN INOCULATIONS	INOCULUM	INCUBATION PERIOD	DURATION OF FEVER	MAXIMUM TEMPERATURE	DAY OF DEATH
					days		
I	25	17	Blood	8	5	104.4	13
	26	17		10	1	103.4	—
	27	control		4	4	104.8	—
	28	control		3	5	104.9	12
II	29	24	Blood	—	—	102.0	8
	30	24		7	1	103.0	—
	31	control		5	3	103.6	22
	32	control		4	4	104.4	10
III	33	35	Yolk sac suspension	3	3	104.6	10
	34	35		4	2	104.4	8
	35	control		3	2	104.4	8
	36	control		3	2	104.5	7

TABLE III

Complement-fixation reactions with Q fever and murine typhus immune guinea-pig serums

INOCULUM	DAYS BETWEEN INOC. AND TESTING OF SERUM	Q FEVER ANTIGEN SERUM DILUTIONS								TYPHUS ANTIGEN SERUM DILUTIONS							
		1:4	1:8	1:16	1:32	1:64	1128:	1:256	1:512	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512
Q fever	17	4	4	4	3	1	0	0	0	0	0	0	0	0	0	0	0
	23	4	4	4	4	4	4	4	2	0	0	0	0	0	0	0	0
	30	4	4	4	4	4	4	2	0	1	0	0	0	0	0	0	0
Murine typhus	17	1	0	0	0	0	0	0	0	4	4	4	2	0	0	0	0
	25	2	0	0	0	0	0	0	0	4	4	4	4	3	3	0	0
	34	0	0	0	0	0	0	0	0	4	4	4	4	4	2	0	0

in the two groups. The most notable result of the infection of the Q fever immune guinea-pigs with the SM strain of murine typhus was the suppression of the testicular reaction. Of the 12 controls 9 developed a moderate to severe testicular reaction whereas of the 12 Q fever immune animals only 2 developed a moderate reaction. Dyer did not note suppression of the testicular reaction in his series of cross-immunity experiments using the American and Australian strains. This result, therefore, constitutes an additional difference in activity between the Panamanian JD strain and others reported.

In guinea-pigs which had recovered from an infection with endemic typhus and which were subsequently inoculated with the JD strain of Q fever in homologous tissue after an interval of 17 to 35 days, a definite prolongation of the incubation period and reduction in the average duration of the febrile reaction was observed. This result is in harmony with that reported by Dyer for the Australian "Q" and endemic typhus "W" strains. Where yolk sac suspensions were employed, an overwhelming infection occurred in both test and control pigs with rapid death of all.

SEROLOGICAL REACTIONS

Etherized antigens were prepared from yolk sacs of chick embryos infected with the SM strain of typhus and the JD strain of Q fever in accordance with the method described by Topping and Shepard (3). These antigens were employed in complement-fixation tests with the serum of immune guinea-pigs. Reference to Table III reveals that although such serums showed high titers with their specific antigens, there was no significant cross-reaction. Bengston (4) similarly failed to find serological cross-reactions between Q fever and typhus immune guinea-pig serums.

SUMMARY

Guinea-pigs recovered from an infection with the SM strain of murine typhus showed a partial immunity against the Panamanian JD strain of Q fever as indicated by prolongation of the incubation period and shortening of the febrile period.

In reverse cross-immunity experiments, guinea-pigs immune to the JD strain of Q fever showed a variable febrile reaction and consistent suppression or modification of the testicular reaction on inoculation with murine typhus rickettsia.

Complement-fixation tests, employing immune guinea-pig serums and yolk sac antigens, showed no significant cross-reactions.

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