ROLE OF AUTOINFECTION IN THE PATHOGENESIS OF PARABIOTIC POISONING

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The results of a bacteriological investigation of allogeneic and syngeneic pairs of parabiotic mice and the results of antibiotic therapy of parabiotic poisoning are described. In mice with parabiotic poisoning the regular development of an enteric autoinfection was observed. In syngeneic parabiosis no autoinfection developed. Treatment with streptomycin and oxytetracycline in the early stages of parabiotic poisoning alleviated the course of the syndrome and prolonged the animals' life. It is concluded that autoinfection plays an important role in the pathogenesis of parabiotic poisoning.

Parabiotic poisoning develops in mice with the greatest constancy if the partners differ in their H-2 histocompatibility locus. The main reason for its development is the graft versus host reaction [2, 3]. Immunological activity of animals exposed to the graft versus host reaction is considerably reduced [4-7]. It is therefore natural to suggest that in parabiotic poisoning an autoinfection may develop, and this may influence the course of the disease.

This paper describes a bacteriological investigation of pairs of parabionts and an attempt to treat the parabiotic poisoning with antibiotics.

EXPERIMENTAL METHOD

Mice of inbred lines CBA (H-2K), C57 Bl/6j (H-2B) and (CBA × C57Bl/6j)F_1 hybrids weighing 17-25 g were used. The animals were joined together into a parabiosis of celomic type. In the experiments of series I, the parabionts were killed with aseptic precautions and seedings were taken from the blood, liver, spleen, and mesenteric lymph glands under sterile conditions on sucrose agar and in sucrose broth for subsequent identification of the isolated cultures. Control seedings were obtained from the same organs of 45 single mice. In series II, from the 5th or 7th day of parabiosis, the mice were given streptomycin and oxytetracycline with their food. Treatment was given daily until the animals died. Control pairs were joined together at the same time as the experimental animals but did not receive antibiotics.

EXPERIMENTAL RESULTS

Typical features of parabiotic poisoning [3] appeared on the fifth to seventh day in the F_1 hybrids during parabiosis with animals of the parental lines and in mice of line C57Bl/6j during parabiosis with CBA mice. The results showing the frequency of seedings of bacteria from the organs of the parabionts are shown in Table 1. Autoinfection was found in 56 of 99 allogeneic pairs (56.6%). Of 56 pairs in which autoinfection was discovered, in 27 (48.2%) the autoinfection was found in only one partner, the one which had the features of parabiotic poisoning; in 22 pairs (39.3%) autoinfection was found in both partners, and in 7 pairs (12.5%) it was found only in outwardly healthy, plethoric parabionts.

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TABLE 1. Infection of Parabionts at Various Times After Union

Series of experiments	Parabiosis	Time of investigation after union	Total number of pairs in experiment	No. of pairs where microorganisms were isolated	Lines of mice from which microorganisms were isolated				P_1	P_2
					only (CBA×C57Bl/6j)F_1	only CBA	only C57Bl/6j	two lines		
					number of mice					
I	CBA c	Before 10th day	18	7	4	1	—	2	<0,01	<0,01
	(CBA×C57Bl/6j)F_1	After 10th day	26	16	8	3	—	5		
II	C57Bl/6j c	Before 10th day	10	4	1	—	1	2	<0,01	<0,01
	(CBA×C57Bl/6j)F_1	After 10th day	28	18	7	—	2	9		
III	CBA c	Before 10th day	8	4	—	—	1	3	<0,01	<0,01
	C57Bl/6j	After 10th day	9	7	—	—	6	1		
	CBA c	Before 10th day	3	1	—	1	—	—		
	CBA	After 10th day	5	—	—	—	—	—		
IV	C57Bl/6j c	Before 10th day	3	—	—	—	—	—		
	C57Bl/6j	After 10th day	5	—	—	—	—	—	—	>0,05
	(CBA×C57Bl/6j)F_1	Before 10th day	3	—	—	—	—	—		
	c (CBA×C57Bl/6j)F_1	After 10th day	5	1	1	—	—	—		
Control: 45 intact single mice (15 mice of each line)			—	—	1	1	—	—	—	—

Legend: P_1 denotes significance of discovery of autoinfection in mice in that series of experiments by comparison with series IV; P_2 denotes significance of discovery of autoinfection in that series compared with control.

TABLE 2. Microflora Isolated From Organs and Blood of Mice During Parabiotic Poisoning

Species of bacteria	No. of bacteria isolated	
	abs.	%
E. coli	48	47,1
B. paracoli	4	3,9
Proteus	6	5,9
Staphylococci	35	34,3
Diplococci	5	4,9
Others	4	3,9

TABLE 3. Effect of Antibiotic Therapy on Course of Parabiotic Poisoning During Parabiosis Between CBA Mice and (CBA × C57Bl/6j)F_1 Hybrids

Expt. No.	Day of parabiosis when antibiotic treatment began	Dose of antibiotics per mouse (in units)		No. of parabiont pairs in experiment	Mean life span (in days)	P
		streptomycin	oxytetracycline			
1	5-й	12 500	5 000	16	20,7±1,3	<0,01
2	7-й	12 500	5 000	10	20,1±0,8	<0,01
Control	No treatment	—	—	17	13,5±1,6	—

In all allogeneic combinations of strains the frequency with which autoinfection was detected increased in the duration of parabiosis and an increase in the severity of the poisoning. Before the tenth day autoinfection was found in 41.7% of pairs, but after the tenth day in 65.1% ($P < 0.05$).

In the syngeneic parabionts, parabiotic poisoning did not develop, as was also the case in the control experiments, and positive seedings from the organs were exceptional.

As Table 2 shows, most of the bacteria isolated belonged to the enteric group or to the staphylococci. Of the total number of the bacteria of the enteric group, 15.5% were identified as enteropathogenic forms of Escherichia coli. In 40% of cultures of staphylococci isolated, evidence of pathogenicity was found (ability to coagulate rabbit plasma, to undergo agglutination in plasma, and to hemolyze sheep's red cells).

Seedings were most frequently positive from the mesenteric lymph glands and liver (69.6%).

After administration of streptomycin (12,500 units) and oxytetracycline (500 units) per mouse to the CBA–(CBA × C57Bl/6j)F_1 parabionts from the fifth or seventh of parabiosis, a marked improvement in the course of the parabiotic poisoning was observed in the F_1 hybrids: the clinical manifestations of the syndrome were less marked and the experimental animals died later than the controls. The increase in the life span of the experimental mice compared with the controls was significant (Table 3).

The results of these experiments show that the enteric autoflora plays an essential role in the pathogenesis of parabiotic poisoning. Penetration of bacteria from the intestine into the internal organs is probably facilitated by destructive and inflammatory changes in the small intestine of the animals affected by parabiotic poisoning [1].

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