CHANGE IN THE ANTIGENIC COMPOSITION OF CERTAIN PARENCHYMATOUS ORGANS IN WHITE MICE INFECTED WITH THE AGENT OF DYSENTERY AND STREPTOCOCCI

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Reports which have recently appeared [1, 2, 3] on the discovery of foreign tissue antigens in a series of pathological processes present great practical and theoretical interest. The formation in the organism of foreign antigen indicates a marked change in protein metabolism due to a far-reaching pathological process. It is not excluded that such antigens may act as the source of pathological reflexes, maintain, exacerbate and complete new symptomatic and pathological bases for disease. Treatment of such a disease which takes into consideration only the original first cause cannot be successful.

Therefore, the discovery of foreign antigens might change our concepts of the pathogenesis of such diseases, or of some of them; determination of the character of the newly formed antigens, and means of rendering them harmless, might radically change the treatment of such diseases.

We believe that changes in protein metabolism are observed in various pathological processes, including infections. They are more extreme, possibly, in prolonged chronic processes, being accompanied by trophic lesions and lending themselves with difficulty to etiotropic treatment.

The aim of our work was to study the possibility of the formation of foreign antigens in the tissues of the liver, spleen, and kidney of white mice, infected separately with sublethal doses of the agent of Flexner dysentery and hemolytic streptococcus.

EXPERIMENTAL METHODS

In all, 8 series of experiments were carried out with guinea pigs. Foreign antigens were demonstrated by the anaphylaxis reaction with desensitization by L. A. Zilber's method.

From white mice, killed with ether, on the 5th day after infection (in one series after 24 hours) we aseptically removed the liver (discarding the gall bladder), the spleen, and kidneys. We ground up the organs finely in a mortar, suspended them in physiological saline, centrifuged the suspension at 2500 rpm. Under the skin of guinea pigs we injected about 1.5 ml of the supernatant liquid, containing from 26.4 to 13.2 mg % protein in 1 ml. After about 21-30 days all guinea pigs of the first 6 series were injected intracardially two or occasionally three times with the fluid corresponding to the organs of healthy mice, at intervals of $1^1/_2$ to 2 hours in doses of 0.2, 0.8 and 1 ml, with the aim of completely desensitizing the animals to the antigens of healthy mice.

About $1^1/_2$ - 2 hours after this we injected, also intracardially, each guinea pig with the original sensitizing material, in a dose equal to that used in the last desensitizing injection, after this we recorded the severity of the anaphylactic response.

Each series of experiments consisted of two variants, and in each variant 4 guinea pigs of about the same weight and the same color.

In the first variant we sensitized the guinea pigs with a suspension from the organs of infected mice with the aim of detecting the formation in them of new antigens; in the second variant the sensitization was carried out with a suspension of the organs of healthy mice with the aim of testing the possibility of the destruction in some of them of contained antigens (or antibodies). In this variant the desensitization was carried out with a suspension of the corresponding organ of infected mice, and the final reaction with a suspension of healthy organ.

In each series of experiments there were controls consisting of 3 guinea pigs. One guinea pig, to exclude the possibility of anaphylaxis due to the agent used to infect the mice, received a subcutaneous injection of a culture of the latter in a dose of 1-2 billion. After 21-30 days the same culture was injected intracardially twice, in increasing doses at intervals of $1\frac{1}{2}$ - 2 hours.

Into the remaining two unsensitized guinea pigs we injected, at the same intervals as those employed for the experimental animals, the corresponding organ suspension to test for toxic properties.

The experiments were carried out by the assistants of our department, E. D. Zhuravlevaya and N. K. Bondarenko, also by V. N. Tarasov and A. M. Gnetnev.

RESULTS OF THE EXPERIMENTS

The results of the experiments given in Table 1 reflect in general the final anaphylactic reaction obtained with the original sensitizing material.

From Table 1 it is evident that the control was in all cases unimpeachable.

The experiments of Series I show a formation of foreign antigens, and a destruction of a certain amount of antigens present, in the livers of mice infected with the agent of dysentery and killed after 24 hours. The experiments of Series II support these findings and at the same time show a direct relation between the duration of the process of dysentery infection in mice and the extent of formation of foreign antigens in their tissues. The data of Series III and IV show the regularity of the formation of foreign antigens in the organism of the mouse infected with dysentery bacilli, it being known that the greatest amount of these antigens are formed in the spleen and kidneys.

In the livers of mice infected with streptococci there is formed a little new antigen and a certain amount of antigen present is destroyed (Series V).

In the spleens of mice similarly infected there is formed a significant amount of foreign antigens and a certain amount of antigen present is destroyed.

Between the degree (strength) of anaphylaxis and the amount of foreign antigen formed there is no correspondence, however there is a close connection, which we took into account in the interpretation of our experiments.

It might be expected that in mice with the most prolonged and severe infections the greatest amount of foreign antigens would accumulate and the anaphylactic reaction in guinea pigs would be stronger and more marked.

In every case of dysentery and streptococcal infection of mice, foreign tissue antigens were formed and there was some, although not significant, destruction of the antigens present; this fact must influence the course of the corresponding infection. It is very probable that the formation of foreign tissue antigen constitutes a fourth indefeasible factor of each chronic infection.

It is very important to know whether specific foreign antigens are formed in the various organs, but from different infections, that is, to what extent there is a universal reaction of the foreign antigens formed.

With this aim Series VII and VIII of experiments were set up with 4 guinea pigs in each series.

Guinea pigs were sensitized with a suspension of the spleen of mice infected with the agent of Flexner dysentery (Series VII) and hemolytic streptococcus (Series VIII) and killed after 5 days. The pigs were desensitized to the antigens of the spleen of healthy mice, after which two of each series received the original

sensitizing material (direct reaction), and the remainder heterologous material (cross reaction). The results of the experiment are shown in Table 2.

TABLE 1

Formation of Antigens in Organs of Infected Mice

Series	Sensitizing Material	Number of desensitized guinea pigs	Final reaction with original sensitizing material			
I	Liver of mice:					
	24 hours after dysentery infection	4	—	+	+++	+
	Healthy	4	+	+	—	+
	Control	3	—	—	—	
II	Liver of mice:					
	5 days after dysentery infection	4	++	++++	+	+
	Healthy	3	+	+	±	
	Control	3	—	—	—	
III	Spleen of mice:					
	5 days after dysentery infection	4	++++	++	++++	++++
	Healthy	4	—	—	—	—
	Control	3	—	—	—	
IV	Kidney of mice:					
	5 days after dysentery infection	4	++++	++++	+	+
	Healthy	4	+	+	+	±
	Control	3	—	—	—	
V	Liver of mice:					
	5 days after streptococcus infection	4	+	+	+	+
	Healthy	4	+	—	—	+
	Control	3	—	—	—	
VI	Spleen of Mice:					
	5 days after streptococcus infection	4	++	+++	+++	++
	Healthy	4	—	++	+	+
	Control	3	—	—	—	

Symbols: + scratching nose with paws; ++ the same and sneezing and ruffled fur; +++ the same and coughing, all clearly expressed; ++++ excitement, convulsions, fatal outcome; —absence of these signs.

From Table 2 it is evident that following dysentery and streptococcal infection there are formed universal foreign antigens.

Thus, in the course of a one day and especially a 5-day infection of white mice with dysentery there is formed in their livers, spleens and kidneys foreign antigens (or antigen), but at the same time in their livers a certain quantity of the antigens present are destroyed. In the course of a 5-day streptococcal infection of white mice in the livers and especially in the spleens there is formed foreign antigens and at the same time a certain

TABLE 2

Examination of the Specificity of Foreign Antigens Formed

Experiment series	Sensitizing Material	Number of desensitized guinea pigs	Final reaction to material	
			Original	Heterologous
VII	Spleen of mice 5 days after dysentery infection	2	++ ++	+++ ++
VIII	Spleen of mice 5 days after streptococcus infection	2	+++++++	++ ++

Symbols as in Table 1.

quantity of the antigens present are destroyed. The antigens formed in the spleens of mice during dysentery and streptococcus infection are not specific.

SUMMARY

When applying active anaphylaxis and desensibilization, it was shown that in the case of experimental dysentery infection of white mice, foreign antigens (or antigen) are formed in their liver, and principally in the spleen and kidneys, whereas a certain quantity of the antigens present are simultaneously destructed. The same phenomenon takes place in the liver, and, particularly, in the spleen of mice being experimentally infected with streptococci.

Foreign antigens formed in the liver of mice in the case of the above infections are nonspecific.

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* In Russian.