THE EFFECT OF EXPERIMENTAL DYSENTERY INTOXICATION ON UREA PRODUCTION IN RATS

R. P. Porfir'eva

Division of Experimental Chemotherapy (Head – Prof. A. M. Chernukh), Institute of Pharmacology and Chemotherapy (Director – Active Member, Acad. Med. Sci. USSR, V. V. Zakusov), Academy of Medical Sciences, USSR, Moscow
(Presented by Active Member, Acad. Med. Sci. USSR, V. V. Zakusov)
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It is well known from clinical practice that dysentery is often accompanied by a change in the functional state of the liver [6, 12]; a disturbance of the antitoxic function of the liver has also been noted [3, 7, 8, 13], but of course, the liver function test for hippuric acid synthesis, ordinarily used in the clinic, does not completely reflect the states of the detoxicating function of the liver. It was therefore of interest to study the effect of dysentery intoxication on other indices of liver function.

Data have been published [8] concerning the effect of dysentery toxin on the capacity of the liver to conjugate phenols, but we have not found any information about the effect of this toxin on so important a function as urea production. When we consider that this process undergoes significant disturbances under other types of toxic influences, such as radiation sickness, prolonged medication sleep, thyrotoxicosis, and exposure to radiation in the far ultraviolet [1, 4, 10, 11], it is to be expected that bacterial toxins will exert a marked effect on it.

In the present study we examined the blood urea content and urea production by liver slices in experimental dysentery intoxication in white rats.

METHOD

The model of dysentery intoxication described by V. I. Mchedlishvili [5] was employed. Complete Flexner's dysentery antigen, obtained from the N. F. Gamaleya Institute of Epidemiology and Microbiology, was injected intramuscularly into white mice weighing 120 – 130 g in a dose sufficient to produce death in 60 – 70% of the animals within three to four days. The animals were examined 24 hours after injection of the antigen. In all, 50 rats were used.

For the blood urea determination the animals were decapitated, 1 ml of blood was placed in a test tube with 1 ml of 20% trichloroacetic acid, and the supernatant fluid was obtained by centrifugation. Urea was determined by the urease method. Soybean extract was used as urease. The urea concentration was expressed as mg% nitrogen.

For the determination of urea production in liver slices, the liver was rapidly removed, slices were prepared in the cold, and after two rinsings slices weighing about 400 mg were placed in Krebs–Ringer–bicarbonate buffer (pH 7.4). NH_4Cl was added to a final concentration of M/100 as an ammonia source, and the slices were saturated for 10 minutes with a mixture of 95% oxygen and 5% CO_2, and then incubated for two hours at 37° with shaking. Proteins were precipitated with trichloroacetic acid, and free ammonia (by Conway's method) and urea were determined in the filtrate. The amount of urea synthesized during incubation was obtained from the difference between the nitrogen concentrations before and after hydrolysis with urease. The urea concentration was expressed in μM nitrogen per gram of wet tissue.

RESULTS

Twenty-four hours after injection of diphtheria antigen, intoxication was outwardly manifested, in the majority of the rats, in a significant reduction of overall activity and activity related to eating, ruffling of hair, dyspnea, and other symptoms. Individual animals were in extremely poor condition with clear-cut signs of impending death (lying on their sides, absence of reaction to external stimuli). Such animals were not used in the experiments with liver slices, but a blood urea determination was made on some of them. They were placed in a separate group.

The results of the blood urea determinations on control rats and rats examined 24 hours after injection of dysentery antigen are shown in Table 1.

It is evident from the data in Table 1 that the mean urea content in the blood of experimental animals was less than that of control animals (control, 16.3 mg%); experimental, 13.2 mg%). The rats mentioned above, which were extremely ill when the blood was taken, were an exception. The urea concentration in the blood of these animals was several times as high as for normal animals (from 39.6 to 103.3 mg%). The condition of these animals should not be considered as resulting from the influence of dysentery toxin alone – it is certain

TABLE 1. Blood Urea Content in the Presence of Dysentery Intoxication, in mg% Nitrogen

No.	Control animals	Animals with dysentery intoxication	
		moderately ill	extremely ill
1	19,0	12,0	85,7
2	10,4	7,8	52,2
3	16,5	11,4	103,3
4	17,2	11,4	39,6
5	17,7	17,4	54,0
6	11,0	14,4	65,4
7	18,9	16,2	—
8	18,3	13,8	—
9	13,8	16,8	—
10	19,8	10,4	—
Mean	16,3±1,06	13,2±1',06	

TABLE 2. Urea Synthesis in Rat Liver Slices in the Presence of Dysentery Intoxication.

No.	Urea content, in μM nitrogen per gram wet tissue	
	controls	animals in a toxic condition
1	65	46
2	56	38
3	57	59
4	45	26
5	41	28
6	44	22
7	67	54
8	77	54
9	69	37
10	49	53
11	45	60
12	—	61
13	—	38
14	—	46
Mean	56±3,7	44±3,5

that other disturbances are also occurring which are characteristic of the agonal state [2]; consequently, the high urea values obtained for these animals probably should be attributed to a disturbance in renal activity, and impairment of urea excretion by the organism.

In the main group of experimental animals, with the usual syndrome of dysentery intoxication, we observed that the blood urea content was lower than in the controls, which is evidence that a disturbance of liver activity had occurred. To ascertain the cause of the reduction in blood urea content, we conducted experiments with liver slices. The results of these experiments are set forth in Table 2.

It is clear from the data of Table 2 that liver slices from normal rats synthesize, on the average, 56 μM urea nitrogen in two hours while the corresponding figure for experimental animals is 44 μM nitrogen (a 22% reduction).

The reduction in urea synthesis by liver slices from experimental animals indicates that dysentery toxin has a depressant effect on urea production by the liver. In the intact organism this is manifested in a reduced blood urea concentration.

Our data thus provide additional material to characterize the effect of dysentery toxin on liver function. In addition to producing a disturbance in phenol conjugation [8] and hippuric acid synthesis [9], this toxin markedly depresses urea production.

SUMMARY

This paper deals with the effect of dysentery intoxication on one detoxifying function of the liver – urea formation – in rats. The experiments showed that the blood urea level in experimental animals is somewhat reduced in comparison with control animals, 24 hours after administration of Flexner's dysentery antigen. Urea synthesis in liver slices from these animals is also reduced, which points to a depressing effect of dysentery antigen on this process.

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