PATHOGENESIS OF DYSENTERY

COMMUNICATION I. EFFECT OF DYSENTERIC INTOXICATION ON THE ASCORBIC ACID METABOLISM OF WHITE RATS

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A serious hindrance to the study of the pathogenesis of dysentery has been the absence of any satisfactory experimental model of dysenteric infection. Introduction of cultures of dysentery germs into laboratory animals does not give rise to the disease in them, and excretion of the bacteria ceases after a few days. It is known that the reason why small laboratory animals cannot be infected with dysentery is related to the intricate complex of mechanisms of natural immunity, not all of which have yet been discovered.

We have, over a number of years [2], been engaged in the study of the distribution of ascorbic acid (AA) in the organs of animals exposed to the action of external and internal factors which affected the reactivity of the organism, and we invariably found that the AA content of the organs deviated from the normal values, and that each separate factor caused a specific change in the pattern of distribution of AA in the organs. We found no change in the ascorbic acid content of the organs when the given factor did not release any of the defense mechanisms of the organism.

In the present paper we describe the results of an examination of the effects on the AA content of various organs, due to administration of dysentery cultures or toxin to white rats, maintained on an adequate and a deficient diet. Changes in the distribution of AA in the organs of the rats were taken as indicators of changes in their reactivity towards the dysenteric infection, and of the effect of dietary factors on the susceptibility of the animals to the given pathogenic agents.

EXPERIMENTAL METHOD

We used white rats for our experiments. The animals were divided into six groups. A dose of 40 billion organisms, taken from a 24-hour agar culture of Flexner dysentery bacteria, was administered through a stomach tube to the rats of the first group (eleven rats), which received the ordinary laboratory stock diet. The rats were killed by decapitation three days later. The second group (six rats), also receiving the stock diet, were given a subcutaneous injection of 2 ml of Boivin's complete antigen prepared from the dysentery bacteria. The animals of the third group (ten rats) were given dysentery culture by stomach tube as well as antigen subcutaneously, at the above dosages. This group was on the same diet as the preceding ones. The fourth group (fifteen rats) served as controls for the first three groups, and received the same diet, but neither culture nor toxin was administered.

The animals of the fifth group (twelve rats) were maintained on a low-protein diet until they had lost 20% of their initial weight, when dysentery culture was given, at the above dosage level; the rats were killed three days later.

Changes in the AA Content (mg %) of Various Organs of Rats, Following Administration of Dysentery Culture or Toxin

Group	Liver		Small intestine		Large intestine		Spleen		Cerebral hemispheres		Kidneys		Suprarenal glands	
	M±m	T	M±m	T	M±m	T	M±m	T	M±m	T	M±m	T	M±m	T
First (stock diet) Given dysentery culture	26.0±1.0	0.8	34.9±2.0	1.7	30.9±1.4	1.5	40.6±2.7	1.0	44.4±1.2	4.3	17.8±1.1	1.1	486.3±26.5	4.0
Second (stock diet) Given toxin	25.5±0.5	0.6	41.2±0.9	4.4	36.9±1.9	3.7	44.6±1.5	3.4	43.8±0.5	5.2	18.2	(n, inadequate)	426.8±	(n-inadequate)
Third (stock diet) Given culture + toxin	30.3±1.5	2.7	42.3±1.0	5.0	33.4±0.9	3.1	48.3±1.1	5.8	45.1±1.5	4.2	20.7±1.6	2.8	456.6±18.7	5.7
Fourth (stock diet) Controls	24.4±1.6	—	29.5±2.5	—	27.2±1.9	—	37.1±1.6	—	37.1±1.2	—	16.4±0.4	—	332.3±27.3	—
Fifth (low-protein diet) Given dysentery culture	17.8±1.1	1.5	32.2±2.3	1.8	26.0±1.6	3.5	38.4±3.1	3.0	40.5±1.2	4.5	14.1±1.3	4.5	386.0±27.6	3.2
Sixth (low-protein diet) Controls	14.6±1.9	—	24.6±3.5	—	17.0±1.9	—	23.7±3.9	—	32.4±1.2	—	7.1±0.8	—	256.3±29.8	—

The sixth group (eleven rats) served as a control for the fifth group; the rats were maintained for the same length of time on the same low-protein diet, but were not given dysentery culture. These rats were killed at the same time as were those of the fifth group. The low-protein diet consisted of casein 3%, corn starch 78%, sunflower seed oil 9%, Osborne-Mendel salt mixture 4%, dry baker's yeast 5% and fish oil 1%.

The following organs were taken for analysis for AA immediately after decapitation, using our previously described method [1]: liver, small and large intestine, spleen, the cerebral hemispheres, the kidneys, and the suprarenal glands.

EXPERIMENTAL RESULTS

It is evident from the results tabulated in the table that most of the organs of rats receiving the stock diet, viz., the liver, small and large intestine, spleen, and kidneys, had the same AA content after administration of dysentery culture as were found in the control group. Significant rises in AA content were found in the brain and in the suprarenal glands.

A much more pronounced reaction was seen after injection of toxin into the rats. In this group, we found significant increases in AA content of the wall of the small intestine ($T = 4.4$) and of the large intestine ($T = 3.7$), of the spleen ($T = 3.4$), and of the cerebral hemispheres ($T = 5.2$). The number of determinations of AA in the kidneys and adrenals was insufficient for statistical treatment. The AA content of the liver remained at normal levels.

A more intense reaction followed simultaneous administration of dysentery culture and toxin. This was manifested by a considerable rise in the AA content of all the organs taken for analysis.

The conclusion may be drawn from our results that the organism of rats is not unreactive either to dysentery bacteria or to dysentery toxin.

Under conditions of protein deficiency the rat organism was found to be far more sensitive to introduction of dysentery culture than was that of rats maintained on the stock laboratory diet. As is evident from the table, administration of dysentery culture was followed by a considerable and significant rise in the AA content of the walls of the large intestine, of the spleen, of the cerebral hemispheres, and of the kidneys, very considerably exceeding the rises in AA content of the same organs after administering dysentery culture, or even toxin, to animals previously maintained on the stock diet.

The results of this experiment provide evidence that dietary factors are of considerable importance in determining the reactivity of small laboratory animals to dysenteric intoxication.

The conclusion may be drawn from the changes in AA content of the various organs that the central nervous system and the adrenal-sympathetic system are the first to be involved in the pathologic process under conditions of mild intensity of attack (administration of dysentery culture to animals on the stock diet). Under more acute conditions (administration of toxin to rats receiving stock diet, or administration of dysentery culture to rats maintained on a protein-deficient diet) the blood cells (as shown by the changes in AA content of the spleen) and the intestines are also affected. The least affected organ is the liver.

In view of our findings regarding the significance of dietary factors in the pathogenesis of dysentery, work has been instituted on this aspect of the problem in monkeys.

SUMMARY

Dynamics of the concentration of ascorbic acid in the organs upon introduction of Flexner dysentery culture, and the total bovine antigen recovered from dysentery bacilli was used as an indicator of the change of reactivity of the organism. In rats receiving a full diet (i.e., animals which are considered nonsensitive to dysentery infection) this test reflects the effect of the central nervous and adrenal-sympathetic systems. Injection of the toxin causes more pronounced reaction with involvement of the blood system and intestines. The effect is much more pronounced when the culture is introduced into rats which were kept for a long time on a diet with low protein content. Thus, the condition of nutrition plays an important part in the pathogenesis of dysentery.

LITERATURE CITED

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