EFFECT OF STAPHYLOCOCCAL TOXIN ON SECRETION AND CHEMICAL COMPOSITION OF THE BILE IN ALBINO RATS

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Among the many problems of infection and immunity, one of particular importance is that of the action of bacterial toxins on the function state of the internal organs and systems of the host. Of the internal organs playing an active part in the irradication of infection, the liver occupies a special place. However, the problem of the effect of bacterial toxins on the many different functions of the liver and, in particular, on the process of bile formation, has received little study.

The object of this investigation was to study the effect of staphylococcal toxin on the bile-forming function of the liver experimentally.

EXPERIMENTAL METHOD

Experiments were carried out on 70 male albino rats. The animals were anesthetized with amylobarbital, the abdomen was opened, and a glass cannula was inserted into the common bile duct and fixed there to collect the bile every hour for the 10 h of the experiment. The rate of bile secretion, expressed in mg/min/100 g body weight, was used as index of the intensity of bile secretion. In addition, the content of water and solid matter in the bile taken every hour of the experiment from 10 rats was determined gravimetrically and the concentration of bile salts (cholates) and of bilirubin was determined colorimetrically.

Staphylococcal exotoxin was obtained by the method of Birsch and Hirschfeld. The toxin used caused death of the rats when injected intravenously in a dose of 1 ml/100 g body weight in a dilution of 1:16. The toxin contained over 4000 minimal hemolytic doses per ml and had well marked hyaluronidase and lecithinase activity.

EXPERIMENTAL RESULTS

Analysis of the control experiment showed that the rate of secretion of bile during observations over a 10 h period gradually diminished on the average from 4.7 ± 0.3 mg/min/100 g during the first hour to 3.5 ± 0.2 mg/min/100 g during the last (10th) hour, and the water content per gram of secretion rose correspondingly from a mean value of 968.9-978.4 mg and the content of solids fell from 31.1-21.6 mg. This decrease took place entirely on account of organic compounds (from 21.4-12.2 mg), mainly of cholates, but not of bilirubin. The results of these experiments served as a basis for comparison with those of the subsequent experiment.

In the next series of experiments on 10 animals the toxin was injected in increasing dilutions—from 1:10-1:5000—in a dose of 0.5 ml/100 g body weight intravenously. The results showed that the toxin in high dilutions had no significant effect on the rate bile secretion. After intravenous injection of toxin in a dilution of 1:20 the rate of secretion was unchanged,but the concentration of cholate was lowered. The indicated depression of cholate formation in the liver. A small increase was also observed in the bilirubin concentration—on the average from 8.0-8.7 go 8.2-11.8 or, in some cases 13.3 mg%.

More marked changes developed after intravenous injection of the toxin in a dilution of 1:10. The rate of bile secretion fell by 33-50%: from 4.7 ± 0.3-2.0 ± 0.2 mg/min/100 g during the first hour from 4.4 ± 0.3-2.7 ± 0.1 mg/min/100 g during the 5th hour, and from 3.5 ± 0.2-2.0 ± 0.2 mg/min/100 g during the 10th hour of the experiment. The bile secretion was still more sharply depressed, especially in the

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second half of the experiment, after intraperitoneal injection of the toxin in a dilution of 1:4 and a dose of 1 ml/100 g body weight. In this case the rate of bile secretion fell from 4.3 ± 0.3-1.9 ± 0.3 mg/min/100 g during the 6th hour and from 3.5 ± 0.2-1.4 ± 0.3 mg/min/100 g during the 10th hour. The content of water and solids was almost unchanged in these circumstances. Nevertheless, the bilirubin concentration rose on the average to 11.6-16.7 mg% after intravenous injection of the toxin and to 13.3-19.3 mg% after intraperitoneal injection.

It was thus shown that staphylococcal exotoxin obtained from the strain Wood-46, when injected parenterally in large doses, caused marked and prolonged depression of the bile-secreting function of the liver in albino rats.

To determine the specificity of action of the staphylococcal toxin on the bile-secreting function of the liver, the toxin in a dilution of 1:10 was first neutralized with specific staphylococcal antiserum and then injected intravenously as in the previous experiments. The results of these tests showed that the staphylococcal antiserum completely neutralized the toxic action of the exotoxin. The rate of bile secretion in this case not only was not depressed, but slightly incresed.

To determined whether this increase in the rate of bile secretion was due to the staphylococcal antiserum or to the formation of products of interaction between the toxin and the specific antiserum, in the last series of experiments the antiserum was injected intravenously in a dilution of 1:10 and a dose of 0.5 ml/100 g body weight. The results of these experiments showed that the antiserum in this dose had no appreciable stimulant effect on bile secretion. It thus follows that the increase in the rate of bile secretion observed after intravenous injection of neutralized staphylococcal exotoxin was caused, not by the staphylococcal antitoxin but to products formed as the result of interaction between the toxin and the specific antiserum.