# INACTIVATION OF PLAGUE MOUSE TOXIN BY THE LIVER AND LEUKOCYTES OF ALBINO RATS

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Administration of carbon tetrachloride and lead acetate to albino rats does not affect their sensitivity to plague mouse toxin, whereas sensitivity to typhoid endotoxin is increased. Death of guinea pigs from plague toxin under similar conditions depends on the presence of ballast lipopolysaccharides in the toxin. Leukocytes of albino rats possess definite detoxicating ability relative to plague toxin.

It is known from the literature that parenterally injected endotoxin is rapidly removed from the circulation and accumulates in organs rich in cells of the reticulo-endothelial system [1, 2, 6], and that blocking of the liver and reticulo-endothelial system sharply increases the sensitivity of the animals to bacterial toxins [4, 5, 8].

To continue the study of the mechanism of action and ways of inactivation of plague toxin in the body, changes in the sensitivity of animals to plague toxin (Baker's fraction 2) and to typhoid lipopolysaccharide were studied after administration of substances blocking the reticulo-endothelial system and liver, and the role of leukocytes in the inactivation of plague toxin also was examined.

## EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on albino rats and mice highly sensitive to plague toxin and on guinea pigs which are resistant to it. $CCl_4$ was injected subcutaneously (0.2-0.4 ml) 48 h before injection of the toxins, and lead acetate was injected intravenously (5 mg) simultaneously with the toxins. Packed leukocytes were obtained by the method of Collins and Wood [3].

The sensitivity of the animals to typhoid toxin was definitely increased in experiments both with $CCl_4$ (by 10-40 times) and with lead acetate (by 15-20 times). Contrary to expectation, virtually no increase in the sensitivity of the albino rats to plague toxin took place: $LD_{50}$ in the control was 18.8 $\mu$g, in the experiments with $CCl_4$ 17 $\mu$g, and 28 $\mu$g with lead acetate.

By contrast to this, the sensitivity of guinea pigs to plague toxin was sharply increased (by 80-100 times) by treatment of the animals with $CCl_4$.

Control tests showed that after inactivation of mouse toxin (fraction 2) by heating (65° for 30 min), the fraction 2 remained just as toxic to guinea pigs treated with $CCl_4$ as the native preparation. Consequently, death of the guinea pigs (intact and receiving $CCl_4$) following administration of fraction 2 was due to the presence of nonprotein impurities in it (lipopolysaccharides), and not to the mouse toxin as previously suggested [7, 9].

The leukocytic reaction to parenteral injection of plague toxin was identical with that in endotoxemia: marked leukopenia during the first minutes of poisoning, increasing in severity until the animal died. After incubation (at 37°) of the plague toxin with packed leukocytes (1 $\mu$g toxin to 0.25-1 million leukocytes), a definite decrease in its toxicity was observed ($LD_{50}$ was increased by 2-3 times). Injection of packed

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leukocytes (40-50 million leukocytes), especially if combined with hydrocortisone (25 mg/kg), gave good therapeutic results (in the group of untreated animals all 17 rats died following injection of 4 $LD_{50}$, while of the 20 rats treated with packed leukocytes, 9 survived).

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