TECHNICAL PAPERS

Effect of Rutin on Anaphylactic and Histamine Shock[1]

R. J. RAIMAN, E. R. LATER, and H. NECHELES

Department of Gastro-Intestinal Research, Research Institute, Michael Reese Hospital, Chicago

In the anaphylactic shock in man and in animals histamine plays an important role, but its liberation does not explain all phenomena observed (*1*). The discovery of rutin as an important tool to affect capillary permeability has given us the means to analyze the role played by capillary permeability in the shock produced in the guinea pig by anaphylaxis and by the administration of histamine.

Medium-sized guinea pigs were sensitized by an intraperitoneal injection of 0.25 cc. of normal horse serum. After a 12-day interval the animals were shocked by a parenteral dose of horse serum.

Series I consisted of 8 animals. These were sensitized and then divided into two groups. Three animals received 2 mg. of rutin intraperitoneally 30–45 minutes before anaphylactic shock was produced. The crystalline rutin was dissolved in 2 per cent NaOH to which 2 per cent acetic acid was added carefully to a point just short of precipitation. The solution was then diluted with distilled water to a volume convenient for injection. The above procedures had to be performed while maintaining the solutions at a temperature below 15° C. to prevent degradation of the rutin. Reaction at higher temperatures was indicated by color changes in the solution.

All animals were then given intracardially a shocking dose of 0.05 cc. of normal horse serum /100 grams body weight. The 3 animals which had received a prior injection of rutin manifested no symptoms. The 5 retained as controls died within 6 minutes, exhibiting the characteristic syndrome of anaphylactic shock in the guinea pig.

Series II consisted of 11 animals sensitized in the previously described manner. These were divided into two groups, one of which, consisting of 5 animals, received 1 mg. of rutin intraperitoneally 30–45 minutes before shocking. The control group received intraperitoneal injections of the same quantity of NaOH and acetic acid solution as used in dissolving the rutin for the first group.

Shocking doses of 0.5 cc. of normal horse serum were administered intracardially to all animals. The 5 which had received rutin showed no signs of shock, while the 6 controls died in 4–10 minutes with typical symptoms of anaphylactic shock.

Series III (11 animals) was subjected to procedures identical with those of Series II except that the solvent for rutin used here was propylene glycol, 0.5 cc. /dose. The controls received injections of the same amount of propylene glycol only.

In this series the 5 controls again died in anaphylactic shock within 10 minutes. Five of the 6 rutinized animals were without signs of anaphylactic shock, while the sixth, which received its shocking dose 60 minutes after the administration of rutin, died in anaphylactic shock in about 15 minutes. Whether this increased time interval between the administration of rutin and its apparent failure to protect is significant has not as yet been determined.

After finding that rutin protected against anaphylactic shock, presumably through its action on capillary permeability, we proceeded to examine the effects of rutin on the shock produced by histamine.

Of a batch of 21 guinea pigs, 6 animals were used to determine the minimal lethal dose of histamine dihydrochloride (donated by Hofmann-LaRoche) injected intracardially or intravenously. Nine animals were given 1 mg. of rutin in 0.1 cc. of propylene glycol intraperitoneally 30–45 minutes before receiving the minimal lethal dose of histamine. The 9 controls received only the propylene glycol.

All animals in both series died within 10 minutes after administration of the histamine, exhibiting the characteristic symptoms of histamine shock.

Our results demonstrate that rutin protects guinea pigs against the fatal effects of anaphylactic shock but not against those of histamine shock. If we assume that rutin protects against anaphylactic shock by virtue of its tightening effect on the capillary endothelium, then histamine may be excluded as the lethal factor of anaphylactic shock. However, in the guinea pig in anaphylactic shock, the dominating picture is that of bronchiolar constriction. In guinea pigs injected 30–45 minutes before the induction of anaphylactic shock with rutin, no spasm of the bronchioles was apparent, and their lungs were found to be normal. On the other hand, injected histamine produced the syndrome of protein anaphylactic shock with bronchiolar spasm and changes in the lungs. A clinical difference between shock induced by either anaphylaxis or by injection of histamine was hardly recognizable.

Another explanation for the protective effect of rutin may be that it prevents the liberation of endogenous histamine, perhaps by unknown factors other than those which increase capillary permeability. The latter explanation seems to be more reasonable because its protective effects on anaphylactic shock are of rather short duration, while its effectiveness on capillary permeability in purpuric disease seems to be more protracted. The latter thought may be sustained also by the findings of Hiramatsu (*2*), who found that guinea pigs were protected against anaphylactic shock by large doses of hesperidin. While the latter preparation may have contained some vitamin P, it may have prevented the liberation of endogenous histamine in a manner similar to that of rutin. Hiramatsu did not report whether hesperidin protected against histamine shock.

References

1. DRAGSTEDT, C. A. *J. Allergy*, 1945, **16**, 69.
2. HIRAMATSU, N. *Jap. J. Derm. Urol.*, 1941, **49**, 304. (Abstr. in *Far Eastern Sci. Bull.*, April 1941, 1.)

[1] Aided by a grant from the Gusta M. Rothschild Fund. The Department is in part supported by the Michael Reese Research Foundation.