The metabolic effect of the drug, apparent for some hours after its administration, had always disappeared by the time the metabolism was determined in the morning about 15 hours after the last dose. The significance of these results is discussed earlier in the paper.

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Relationship Between Peptone Shock and Anaphylactic Shock.

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We have recently reported that the intravenous injection into dogs of a solution of peptone produces shock indirectly by leading to the liberation of a vasodepressor substance, identified as histamine, from the tissues.[1] Thus the mechanism of peptone shock is apparently similar to that of anaphylactic shock.[2] Biedl and Kraus[3] pointed out the remarkable similarities between these conditions. They also reported that peptone shock desensitizes an animal to anaphylactic shock and *vice versa*. They concluded that the fundamental mechanism concerned in these reactions was identical. They interpreted the reactions as indicating that peptone contains some active substance, such as Popielski's vasodilatin, which can produce shock directly, and that in the anaphylactic experiment a mother substance is formed as the result of the sensitization which then discharges this active peptone constituent when the shocking injection of antigen is made. Subsequent investigators have had variable results in attempting to influence an anaphylactic reaction by the prior administration of peptone. Hill and Martin[4] in their review summarize the reports as follows: "In short, there is some, but not striking evidence that peptone may inhibit shock within certain defined limits."

In view of our demonstration that both peptone shock and anaphylactic shock are reactions that are brought about indirectly by

[1] Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Therap.*, 1937, **59**, 429.

[2] Dragstedt, C. A., and Mead, F. B., *J. Pharm. and Exp. Therap.*, 1936, **57**, 419.

[3] Biedl and Kraus, *Wien. Klin. Wchnschr.*, 1909, **22**, 363.

[4] Hill, J. H., and Martin, L., *Medicine*, 1932, **11**, 141.

the liberation of histamine from the tissues of the shocked animal, the relationship between these reactions has considerable significance. For example, the question whether desensitization is related to a depletion or exhaustion of the mobilizable store of histamine in the tissues is subject to direct approach by such a study. The present investigation, therefore, was undertaken in the effort to determine whether or not one reaction would desensitize to the alternative reaction.

Dogs were sensitized by the injection of 5 cc. of horse-serum intravenously and 5 cc. subcutaneously. After incubationary periods of 14 or more days, they were anesthetized with ether and barbital, the carotid cannulated for recording blood pressure, and the femoral vein exposed for injections. In 20 animals anaphylactic shock was provoked by the intravenous injection of horse serum, and then, after recovery peptone was injected. Definite shock reactions occurred in all, 5 being fatal. In 16 animals peptone shock was induced first and the specific anaphylactic reaction second. Shock occurred in all but 3.

It is quite apparent from the results obtained that crossed desensitization between peptone shock and anaphylactic shock is not complete in either direction. Thus it is obvious that desensitization is not accounted for on the basis of an exhaustion of the available supply of histamine in the tissues. We have been able to demonstrate the presence of histamine in the blood following the second type of reaction although it had previously appeared and then disappeared as the result of the preceding reaction. It is also indicated that anaphylactic shock is not brought about by the formation of an intermediary substance which exists preformed in peptone solutions since if such were the case crossed desensitization should be as complete as uncrossed. There is some indication that preceding reactions of one kind may diminish slightly the severity of the alternative reaction. The peptone-anaphylaxis experiment is somewhat comparable to a multi-sensitization experiment in which an animal has been simultaneously sensitized to several antigens and the subsequent injection of one antigen decreases but does not abolish the response to the remaining antigens. It does not seem unreasonable to suppose that the diminution in severity of such reactions may be related to a reduction in the available supply of histamine in the tissues but complete homologous desensitization can not be explained upon such a basis.